



Ministero della Salute

DIPARTIMENTO DELLA SANITA' PUBBLICA E DELL'INNOVAZIONE DIREZIONE GENERALE DELLA RICERCA SANITARIA E BIOMEDICA E DELLA VIGILANZA SUGLI ENTI

IL MINISTRO

VISTI gli articoli 12 e 12 bis del Decreto legislativo 30 dicembre 1992, n. 502, e successive modificazioni ed integrazioni, che disciplinano lo svolgimento delle attività di ricerca corrente e finalizzata in ambito sanitario e individua i soggetti che possono concorrere alla realizzazione dei relativi progetti di ricerca;

VISTA la legge 23 dicembre 2009, n.192 concernente il bilancio di previsione dello Stato per l'anno finanziario 2010 e bilancio pluriennale per il triennio 2010-2012;

VISTO il decreto del 27 settembre 2011, registrato dall'Ufficio Centrale del Bilancio presso questo Ministero in data 30 settembre 2011 n. 5292, con il quale è stata impegnata la somma di euro 85.627.000,00 per il finanziamento delle spese per la ricerca finalizzata in attuazione degli obiettivi prioritari, biomedici e sanitari del Piano Sanitario Nazionale;

VISTO il Bando Ricerca finalizzata 2010 pubblicato in data 29 settembre 2011 il quale dispone, al punto 3, la procedura di valutazione dei progetti presentati;

CONSIDERATA la necessità di dover costituire la commissione per la Study Section relativa alla valutazione dei "progetti presentati da giovani ricercatori", di cui al medesimo bando di ricerca finalizzata 2010;

VISTO l'articolo 2 comma 316 della Legge 24 dicembre 2007, n. 244 (Legge Finanziaria 2008), che modifica il comma 814 articolo 1 della legge 27 dicembre 2006 n. 296 destinando una quota non inferiore al cinque per cento relativamente all'anno 2007 e al dieci per cento a partire dal 2008, ai progetti di ricerca sanitaria svolta dai soggetti di cui all'art.12 bis, comma 6, del citato decreto legislativo n.502/1992, presentati da ricercatori di età inferiore ai quaranta anni, valutati da uno specifico Comitato.

CONSIDERATO che il citato articolo 1, comma 814, della legge n. 296/2006, modificato dall'articolo 2 comma 316 della Legge 24 dicembre 2007 n. 244, demanda l'attuazione della stessa disposizione ad apposito decreto del Presidente del Consiglio dei Ministri di concerto con il Ministro della Salute ed il Ministro dell'Istruzione dell'Università e della Ricerca;

VISTI i commi 1 e 2 dell'art. 5 del DPCM del 27 luglio 2007, registrato alla Corte dei Conti il 5 settembre 2007 al registro 9 nove foglio 273, in cui si individua la composizione del Comitato di

valutazione dei progetti presentati dai giovani ricercatori – composto da dieci ricercatori, di nazionalità italiana o straniera, di età inferiore ai quaranta anni, di cui due nominati su designazione del Ministero dell'Istruzione, dell'Università e della Ricerca - e il comma 3 del medesimo articolo in cui si prevede la nomina del Presidente di detto Comitato da parte del Ministro della Salute;

VISTO l'art 5 del sopracitato DPCM del 27 luglio 2007 in cui si prevede, al comma 4, la possibilità da parte del Comitato di avvalersi di esperti esterni, ed al comma 5, la prevalenza del voto del Presidente in caso di parità in sede di decisione finale all'esito del processo di valutazione;

VISTO l'art 5, comma 6, del DPCM 27 luglio 2007 in cui sono disciplinati eventuali conflitti d'interesse da parte di membri del Comitato e i presentatori dei progetti da valutare;

VISTA la nota del Ministero dell'Istruzione, dell'Università e della Ricerca del 18 aprile 2012, che designa i rappresentanti del medesimo Ministero in seno al predetto Comitato di Valutazione;

RITENUTO che il Dottor Ennio Tasciotti è in possesso dei requisiti per presiedere il menzionato Comitato;

DECRETA

Art. 1

(Composizione Comitato di Valutazione)

Il Comitato di valutazione Giovani Ricercatori di cui alle premesse è così composto e la sua durata è correlata ai lavori di definizione dei progetti e dei relativi finanziamenti:

N	Nome e Cognome	Istituzione presso cui il Ricercatore svolge l'attività
1	Ennio Tasciotti	Department NanoMedicine The Methodist Hospital Research Institute 6670 Bertner Avenue Suite R7-114 Houston Texas, 77030
2	Piergiorgio Mastroberardino	Genetics Department - Erasmus Medical Center Room Ee 1928 - Dr. Molewaterplein 50 3015 GE Rotterdam The Netherlands
3	Stefania Mondello	Banyan Biomarkers, Inc. 13400 Progress Boulevard Alachua, Fl 32615 Usa
4	Davide Cattano	The University of Texas Medical School at Houston Department of Anesthesiology 6431 Fannin MSB 5.020 Houston, Texas 77030
5	Marco Pravetoni	Minneapolis Medical Research Foundation Hennepin County Medical Center 600 Fred L. Shapiro Building, 914 South Eighth Street -Minneapolis, MN 55404
6	Federico Soldani	Division of Epidemiology Office of Surveillance and Biometrics, CDRH US Food and Drug Administration (FDA) 10903 New Hampshire Ave. White Oak 66/4270 - Silver Spring, MD 20993-0002

7	Chiara Gabbi	University of Houston Department of Biology and Biochemistry Center for Nuclear Receptors and Cell Signaling 3605 Cullen Blvd Houston – TEXAS 77204 - USA
8	Emanuela Ricciotti	Institute for Translational Medicine and Therapeutics University of Pennsylvania 3400 Civic Center Boulevard Philadelphia, PA 19104
9	Gino Cingolani	Dept. Of Biochemistry and Molecular Biology Thomas Jefferson University Philadelphia, PA
10	Giampiero Giovacchini	Institut fur Radioonkologie und Nuklearmedizin Stadspital Triemli Birmensdorferstrasse 497 Zurigo (Svizzera)

Il Comitato è presieduto da Dott. Ennio Tasciotti.

In sede di decisione finale all'esito del processo di valutazione, in caso di parità prevale il voto del Presidente.

Art. 2
(Procedure e incompatibilità)

Il Comitato di valutazione Giovani Ricercatori, provvede a redigere un elenco, in ordine decrescente di merito, di tutti i progetti in base al punteggio complessivo dei revisori, come previsto al punto B1) del bando.

Il Comitato di valutazione Giovani Ricercatori, al fine del contenimento dei costi, potrà effettuare riunioni utilizzando anche le procedure di videoconferenza.

La Commissione di valutazione Giovani Ricercatori ai fini della valutazione dei progetti può avvalersi, nel caso insorgano controversie, di ulteriori revisori come previsto dal Bando.

Gli appartenenti al Comitato di valutazione Giovani Ricercatori, nell'accettare l'incarico, si impegnano al rispetto di quanto previsto dal comma 6 dell'art 5 del DPCM 27 luglio 2007, citato in premessa, e in particolare ad astenersi dalle valutazioni dei progetti proposti da ricercatori con i quali sia in atto o sia stata svolta una documentata collaborazione scientifica.

Art. 3
(rimborso spese)

Ai componenti del Comitato di valutazione Giovani Ricercatori non spetta alcun compenso. È previsto solo il rimborso delle spese di viaggio e di soggiorno, che per i componenti e gli esperti estranei alle Amministrazioni dello Stato è equiparato a quello spettante ai dirigenti generali delle stesse.

Art. 4
(Spese di funzionamento)

Gli oneri derivanti dalla costituzione ed il funzionamento del Comitato di valutazione Giovani Ricercatori saranno addebitati sul capitolo 3125 piano gestionale 6 – “Spese per la costituzione ed il funzionamento del comitato di valutazione dei progetti di ricerca sanitaria presentati da giovani ricercatori”.

Art. 5

Il presente decreto è trasmesso agli Organi di controllo per la relativa registrazione.

Roma, li 23 APR. 2012

IL MINISTRO
(Prof. Renato BALDUZZI)



UFFICIO CENTRALE DEL BILANCIO
presso il MINISTERO DELLA SALUTE

Registrato con presa d'atto n° 575
Roma 24/04/2012

IL DIRETTORE DELL'UFFICIO CENTRALE
DEL BILANCIO





Ministero della Salute

DIPARTIMENTO DELLA SANITA' PUBBLICA E DELL'INNOVAZIONE
DIREZIONE GENERALE DELLA RICERCA SANITARIA E BIOMEDICA E DELLA
VIGILANZA SUGLI ENTI

COMMISSIONE DI VALUTAZIONE GIOVANI RICERCATORI

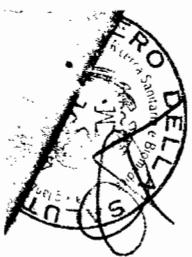
BANDO R.F. 2010

(ex D.M. 23 aprile 2012)

VERBALE STUDY SESSION

2 – 3 – 4 MAGGIO 2012

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I giorni **2, 3 e 4 maggio 2012** alle ore **9,00**, presso la Stanza A325 del Ministero della Salute, sito in Roma in Via Giorgio Ribotta, 5, si è riunito il Comitato di Valutazione per i progetti presentati dai Giovani Ricercatori afferenti al Bando R.F. 2010, nella composizione di cui al D.M. 23 aprile 2012.

Partecipano i componenti di seguito riportati:

Dott. Davide Cattano

Dott. Gino Cingolani

Dott.ssa Chiara Gabbi

Dott. Giampiero Giovacchini

Dott. Pier Giorgio Mastroberardino

Dott.ssa Stefania Mondello

Dott. Marco Pravetoni

Dott.ssa Emanuela Ricciotti

Dott. Federico Soldani

Dott. Ennio Tasciotti

Il *Dott. Massimo Casciello*, Direttore Generale della Ricerca Sanitaria e Biomedica e della Vigilanza sugli enti, porge il benvenuto ai presenti e illustra il lavoro del Comitato, comunicando che, ai sensi del suddetto D.M. 23 aprile 2012, il Sig. Ministro ha nominato il Dott. Tasciotti Presidente del suddetto Comitato.

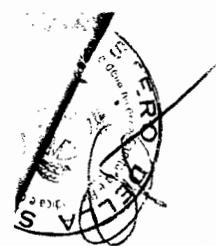
Presenta, quindi, il *Dott. Gaetano Guglielmi*, Direttore dell'Ufficio 3 di questa Direzione Generale referente per il sistema informatico del processo di valutazione e la *Dr.ssa M. Novella Luciani*, Direttore dell'Ufficio 4, referente per i dettagli organizzativi e per i rapporti nella fase audit con la Commissione Nazionale per la Ricerca Sanitaria.

Il *Dott. Gaetano Guglielmi*, illustra le procedure di assegnazione e di valutazione dei progetti effettuate dai referees dei progetti giovani ricercatori presentati nel Bando Ricerca Finalizzata 2010.

I progetti presentati in questa sezione del Bando sono in totale 977 e le risorse economiche messe a disposizione dal bando per questa area sono pari a Euro 30.627.000,00.

Illustra preliminarmente le procedure da seguire nel corso della study session e, presentata ai componenti la situazione del referaggio effettuato, vengono precisate le modalità di accesso al sistema, per le quali sono attribuite a ciascun componente le proprie credenziali informatiche.

 2



Il **Dott. Ennio Tasciotti**, preso atto dell'elenco dei progetti con le valutazioni senza face to face concluso (allegato 1), propone di soffermarsi sui quattro progetti in lista che presentano una sola valutazione e che, in accordo con i commissari, vengono assegnati per una seconda valutazione a singoli componenti del Comitato secondo la seguente distribuzione:

- GR 2010 2306977 dott. Tasciotti
- GR 2010 2318142 dott. Cattano
- GR 2010 2315743 dott. Soldani
- GR 2010 2318089 dott.ssa Gabbi.

I commissari, valutati i progetti, relazionano al Comitato e condividono la valutazione e il punteggio finale.

Il Comitato, confermate le medie dei progetti con due valutazioni con punteggi simili, prosegue con la valutazione dei restanti progetti che, pur avendo tutti due giudizi, evidenziano un delta tra i punteggi > 3 e che necessitano di ulteriore verifica da parte del comitato (allegato 2).

I componenti aggiornano le valutazioni individualmente, comunicando i propri punteggi e le relative motivazioni (allegato 3).

Conclusa questa fase di valutazione, viene visualizzata la situazione completa della nuova graduatoria dei progetti.

Il Comitato suggerisce quindi, tenuto conto dell'elevata qualità scientifica dei progetti presentati, di assicurare il finanziamento di tutti i progetti con un final score pari a 8.5, ritenendo che la necessaria riduzione economica, applicata in modo lineare a tutti i progetti finanziati, non infici la loro realizzazione.

Dopo ulteriore verifica della coerenza del giudizio espresso con il punteggio attribuito, il Comitato di Valutazione "Giovani Ricercatori" collegialmente procede alla stesura della graduatoria finale, approvandola, come da allegato 4 che fa parte integrante del presente verbale.

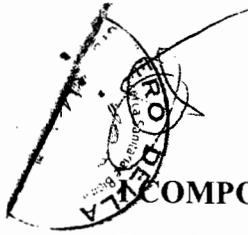
Infine il Comitato di Valutazione approva le graduatorie dei progetti Giovani Ricercatori Esteri e Giovani Ricercatori Cofinanziati di cui ai rispettivi allegati 5 e 6 che fanno parte integrante del presente verbale.

Il Presidente chiude i lavori della study session del Comitato di Valutazione dei progetti Giovani Ricercatori alle ore 20,00 del 4 maggio 2012.

Roma, 4 maggio 2012

IL PRESIDENTE

Dott. Ennio Tasciotti



COMPONENTI:

Dott. Davide Cattano

Dott. Marco Pravetoni

Dott.ssa Chiara Gabbi

Dott.ssa Emanuela Ricciotti

Dott. Gino Cingolani

Dott. Pier Giorgio Mastroberardino

Dott.ssa Stefania Mondello

Dott. Giampiero Giovacchini

Dott. Federico Soldani

BANDO RICERCA FINALIZZATA-GIOVANI RICERCATORI 2010

COMITATO VALUTAZIONE GIOVANI RICERCATORI Elenco Motivazioni

GR-2010-2298984

Serine racemase: an emerging therapeutic target for the treatment of schizophrenia and neurodegenerative diseases.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:10.75

GR-2010-2299663

Study of a Novel RNA-mediated Transcriptional Activation mechanism, Called RNA Memory as Therapeutic Strategy for Human Diseases.

This project is based on an innovative idea regarding RNA memory as factor involved in the pathogenesis of cancer, genetic diseases and in senescence. It lacks strong literature support. Moreover, the aims should be more specific (for instance, only focusing on carcinogenesis) and have both in-vitro an in-vivo approach. The PI is biologist, PhD but he does not have a good track of publications. An additional review was performed. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:22

GR-2010-2300648

Obesity and inflammation: new mechanistic insights from whole exome sequencing and analysis of microRNA regulation by polyphenols.

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2300649

Implementation of cell treatments for untractable immune disorders. Correlation of immunomodulatory potency of BM-MSC to the patient's immune activation and development of custom licensing strategies.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.0

GR-2010-2301880

Novel targets of cocaine and amphetamine influencing intercellular communication mechanisms

Reviewers expressed discording evaluations As a result, F2F was performed but it wasnt well documented so the review scientific committee perform a new evaluation.

Scientific quality and relevance of the research : Recent studies suggest that G-protein coupled receptors (GPCRs) can aggregate to form heteroligomers within lipid rafts. Lipid rafts have a possible role in neuroplasticity and alterations induced by cocaine and amphetamines, as well as opioids and other GPCR agonists Score: 3

Innovation and originality of the project (relative to the current international literature) : The project is original and innovative, although it fails to assess the relevance of lipid raft system to behavioral effects or at least neurochemical effects of cocaine and amphetamine. The application suggested that these studies would be helpful to identify novel treatment. Since few experimental therapies are available or at least being studied at pre-clinical level, the PI should discuss those so that studies could target specific receptors within GPCR. Score: 5

Methodology and development strategy of the project (over its three-year duration), preliminary data and bibliographical reference : The proposed studies are based upon state-of-the-art in vitro and cellular-based assays. However, this methodology would gain from employing or include some in vivo models. For instance, mice or rats could be exposed to cocaine or amphetamine in vivo and then some studies performed in primary neuronal cultures. Mosts of neuroplasticity occurs after in vivo exposure therefore in vitro-induced adaptation do not necessarily translate. For instance, cocaine and amphetamine concentrations should be compared (and justified by a literature review) to in vivo concentrations found in rodent and/or human brain. Score:3

Profile of the Investigator and his/her scientific work Text: The profile of the investigator is adequate, although it is not clear if the PI is yet an independent investigator. Score: 6

Final assessment : The project is innovative and interesting, although it does not provide insights to the relevance of the observed in vitro measures to in vivo parameters. Studies would gain critical relevance by introducing at least a model of in vivo exposure to cocaine and amphetamines. Most neuroplasticity alterations are induced by in vivo exposure (including lipid rafts rearrangements, or cytoskeleton modifications) so in vitro exposure is quite limited. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:17

GR-2010-2302822

IL-21-mediated dysregulation of FoxP3 promotes resistance to tolerance in transplantation

Reviewers expressed discording evaluations of 5 and 17, although F2F discussion was appropriate and well documented. The scientific review committee agrees on F2F final score.

GR-2010-2303136

EVALUATION OF EFFICACY AND SAFETY OF FLAVOCOXID, A CATECHIN AND BAICALIN FLAVONOIDS ASSOCIATION, IN THE MANAGEMENT OF METABOLIC SYNDROME: A PRECLINICAL AND CLINICAL STUDY

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2303444

TARTEGED TREATMENT OF HAIRY CELL LEUKEMIA

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2304111

Mucus Layer Component (Muc2) Contribute to Shape the Intestinal Immune Response

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2304481

An improve of tumor regression with a cancer-risk modulated radiochemotherapy in local advanced rectal cancer (LARC) can lead to avoid doing major surgery: a randomized phase II study.

An additional review was performed. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:26.25

GR-2010-2304892

Human Well-Being: a Twin Study on the Relation between Optimal Psychological and Biological Functioning

The committee has re-evaluated the project and the score given by the two reviewers during the F2F discussion is collegially confirmed.

GR-2010-2304917

Development of pharmacological strategies for the personalization of anti-leukemic therapy for pediatric acute lymphoblastic leukemia

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2304924

Molecular characterization of IFI16 protein: development of new diagnostic and therapeutic tools for autoimmunity

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2304946

Contribution of fibroblast-derived microRNAs to prostate and lung cancer aggressiveness

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.75

GR-2010-2305090

MELANOMA-TARGETING MULTIFUNCTIONAL NANOPARTICLES FOR THERAGNOSTIC APPLICATIONS

Reviewers initially expressed discording evaluations. An additional evaluations was performed. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2305144

Cancer predictivity of biomarkers of exposure: an occupational-based approach

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.0

GR-2010-2305373

SCREENING OF SOMATIC MUTATIONS IN ADVANCED STAGES LUNG ADENOCARCINOMA THROUGH NEXT GENERATION DNA SEQUENCING

The concerns brought up by the less enthusiastic review about the methodology as well as the overambitious nature of the project are understandable. The mathematical average (11.25) is therefore appropriate. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:11.25

GR-2010-2305443

Non-invasive stimulation of cerebello-thalamo-cortical circuits in dystonic patients

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2305546

Mitochondrial Carrier Diseases: Clinical prevalence, study of pathogenetic mechanisms, and possible therapies

The project is very similar to a previous application presented in the 2009 senior call (RF-2009-1473187), under the lead of a talented, experienced, and established investigator (Dr. Santorelli). It is questionable whether the applicant, who is at relatively early stages in his career, has developed sufficient skills to handle this ambitious project. The involvement of several research centers does not facilitate the task. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.0

GR-2010-2305717

Perinatal life-threatening arrhythmias and Sudden Infant death

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:8.5

GR-2010-2305867

New predictive markers of response to chemoradiotherapy in rectal cancer: microRNA-17-92 and methylation profile

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:16.5

GR-2010-2305907

Modulation of immune (T cell) response to islet autoantigens by human mesenchymal stem cell-derived microvesicles

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:13.0

GR-2010-2306342 Glutamate abnormalities in obsessive compulsive disorder: Neurobiology, Neuroimaging, and Genetics.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:18.75

GR-2010-2306432

Generation and characterization of an antiCD56-IL15 immunocytokine for functional reconstitution of NK cells in HIV infection

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:6.25

GR-2010-2306447 Large scale exome sequencing in familial and sporadic amyotrophic lateral sclerosis.

The reviewers gave discording evaluations of 4 and 16. However, the reviewer scoring 4, did not provide any comment at all or justification no participated to F2F. The scientific review committee re-evaluated the proposed studies and found the reviewer code 1711369 (score 16) evaluation more appropriate. The project is innovative and interesting, however aims are overachieving and too ambitious. Too many studies are proposed without clear analysis on expected outcome. The main concern is that a young PI will not be able to coordinate and manage such a huge amount of workload and data. The PI should resubmit the proposed studies with a narrower focus. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:16

GR-2010-2306509

Animal breeding and functional food to improve human health.

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2306755

Gene-environment interaction in top-down regulation of compulsive eating: a translational study of food addiction

both reviews have merits and although the score is significantly different between the two reviews. As a result, F2F was performed but it reported same critiques reviewers code 1710741 (14.5) with different score without clarifications. So the review scientific committee decides to evaluate the project. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.25

GR-2010-2306756

MitoCure: developing treatments for mitochondrial diseases

A strong proposal by a well trained and productive pl. The working hypothesis is strong and the research approach well developed (although, to some extent, challenging). Given the PI impressive publication record and strong network of collaborators, it is plausible the PI will be able to carry out the proposed research. The more negative scores by reviewer (code 1710853) are not fully justified by his/her critiques, raising concerns over the significance of these scores. This project received an additional critique. Thus, after attentive re-exam, the committee proposes to take the average score between reviewer code 13003212 and code 1711631. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:6.25

GR-2010-2306770

Development of a prognostic tool based on a systems biology approach to identify new predictive markers of the evolution of different diseases

Reviewers initially expressed discording evaluations. An additional evaluations was performed. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2306876

Investigation of brain functional connectivity by graph-based network analysis: application to normal ageing and prodromal Alzheimers disease.

Reviewer code 1710585 accepts in F2F 9 without discussion -Reviewer code 1710585 gives is too ungenerous in the score of PI -Main concern: The PI state that patients will be recruited at 3 different institutions (Milan, Rome and Brighton). The PI also states that 40 subjects will be recruited and does not specify whether each recruiting center will have its own control subjects. There is no justification to the need of the additional recruiting in Rome and England since the number of pts planned to be recruited in Milan (where PI is resident) is 200 which appears to suffice for the data analysis. The proposal contains no information on characteristics of the MR scanners and used sequences so that averaging of brain studies obtained with differ centers will be confusing. Overall the project appears very ambitious as many studies are planned (fMRI, diffusion MR, EEG, MEG). The scientific review committee agrees on F2F final score

GR-2010-2306977

Liposome-delivered siRNAs inhibition of PTG in Lafora Disease: a model of innovative strategy for treatment of neurometabolic diseases

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:11.25

GR-2010-2307044

Role of calcineurin/Nuclear Factor Activated in T cells (NFAT) activation in leukemogenesis

Reviewers expressed discording evaluations. An additional evaluations was performed. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:13.25

GR-2010-2307183

Analysis of development and persistence of protective immunity after new and routine vaccinations in primary and secondary immunodeficiencies

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2307215

Radiolabelled nanoparticles as radiopharmaceuticals for preclinical drug development with molecular imaging in angiogenesis

Reviewers initially expressed discording evaluations. An additional evaluations was performed. As a result, F2F was performed and it wasn't well documented After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score: 9.0

GR-2010-2307275

Predictive markers of bone metastasis in primary breast tumors

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.75

GR-2010-2307421

Early non invasive molecular diagnosis of prostate cancer: role of cell free DNA in blood and urine

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:15.75

GR-2010-2307511

Experimental intra-tonsillar prion infection in sheep: a pathogenetic insight into classical and atypical scrapie propagation.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:11.0

GR-2010-2307608

Postmenopausal Womens Bone Health: A Novel Approach to Prevent fragility fracture

Reviewers expressed discording evaluations, an additional evaluations was performed. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:16.0

GR-2010-2307655

Lipidomic investigations in Multiple Sclerosis: research of molecular biomarkers

Reviewers expressed discording evaluations, an additional evaluations was performed. This is very well-written project, has a structured design with no major flaws. The PI and his team are qualified and they have the necessary skills to carry out the project as proposed. On these premises, the commission proposes to raise the final score to increase the chances of funding. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:8.5

GR-2010-2307929**BORON NEUTRON CAPTURE THERAPY (BNCT) IN CUTANEOUS RECURRENCES OF BREAST CANCER: THE DIAGNOSTIC AND THERAPEUTIC UTILITY OF 18F-FBPA PET/CT**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on F2F final score 9.0

GR-2010-2307992**The dietary and genetic protection to coronary artery disease**

The committee doesn't agree with the final score suggested by both reviewers. The reviewers found several weaknesses in the study design of the proposal and suggested an initial score of 11 and 12. Then, in the face to face the reviewers agrees to assign the final score of 8, without a detailed justification. The committee observed a major limitation in the study designed by Dr Romeo. The PI didn't consider the importance of the prognostic factors like drug therapy and ethnicity in the study design. No preliminary data were provided. On these premises, and after having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:11.5

GR-2010-2308044**ADAM17/TIMP3 axis modulates immune cell activation in a model of neurovascular dysfunction**

The concerns of the less positive review about the methodology and its overambitious nature are fully justified and understandable. The mathematical average (10.5) is appropriate and should be considered as a generous evaluation. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:10.5

GR-2010-2308100**Targeting strategies in Numb-defective cancers**

After careful consideration of the reviewers comments, the review panel fully agrees with the score reached in the F2F process.

GR-2010-2308107**Towards controlling paratuberculosis in cattle through marker assisted or genomic selection**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:18.75

GR-2010-2308132**The pathophysiology of alpha-synuclein toxicity and infectivity in Parkinsons disease: molecular mechanisms and therapeutic implications**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:15.5

GR-2010-2308134**Glycated haemoglobin and fasting blood glucose concentration: distribution, time trends and prediction of cardiovascular diseases in the Italian adult population**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it wasn't well documented After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.0

GR-2010-2308269**A population genetics approach to identify novel susceptibility alleles for chronic inflammatory conditions: application to multiple sclerosis and inflammatory bowel disease**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2308399**CNF1 as a new therapeutic approach for the treatment of astrogliosis and neuroinflammation in Alzheimer's disease**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.75

GR-2010-2308622**Cdk5 in tumor progression.**

The committee has re-evaluated the project and its assessments. This research project, presented by a young investigator, aims to investigate the role of Cdk5 during carcinogenesis. The committee feels that the methodology in aim 1.3 appears to be very weak. In particular the investigator should carefully define and justify the type of cancer selected for the study, the group of cancer patients/controls with precise selection and exclusion criteria. Therefore, the committee confirms the F2F final score decided by the two reviewers.

GR-2010-2308713**Development of innovative methods for radiobiological optimization of radio-nuclide therapy treatments**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2308715**Hepatitis E: break the chain between animals and human**

Reviewers initially expressed discording evaluations. An additional evaluations was performed. As a result, F2F was performed. The scientific review committee agrees on final score 15.5

GR-2010-2308995**Manufacturing information of orthopedic articular prosthesis. Analysis of specific safety issues for radiotherapy, magnetic resonance, orthopedic surgery and identification of a traceability model.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. Interesting and relevant proposal of clinical-management value and direct implications for public health. The scientific review committee agrees on F2F final score

GR-2010-2309009**NMDA-based pharmacotherapy associated to cue exposure therapy: a potential treatment for nicotine relapse**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:16.5

GR-2010-2309041**Boosting intratumor tertiary lymphoid structures with IL-7 and LT-alpha, to stimulate the immune response against pancreatic cancer.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:11.25

GR-2010-2309046**Isolation, characterization and pre-clinical evaluation of cell-derived microparticles as therapeutic tools in immunological and genetic disorders.**

The field of Exosomes and Cell-Derived MicroParticle technologies for translational research in regenerative medicine is a great field in rapid growth. The PI is well positioned to conduct such research and the grant is well written. The reviewers mainly evaluated differently the degree of expertise of the PIs and in particular one of the reviewers has been unfair in the score assigned to the PI. The reviewers committee has assigned a final score of 10 to this project.

GR-2010-2309052**Analysis of RNA processing defects in amyotrophic lateral sclerosis**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:11.75

GR-2010-2309071**Neurological and visual impairment in Cobalamin C defect: a novel therapeutical approach based on antioxidant therapy**

The reviewers provided contrasting feedback; nevertheless, both referees motivate the assigned score appropriately. Additional reviewer finds the research approach of WP2 (Redox proteomic studies) less well developed than WP1. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:15.5

GR-2010-2309418**Role of Che-1 in DNA damage response**

After careful consideration of the reviewers comments, the review panel fully agrees with the score reached in the F2F process.

GR-2010-2309463**ROLE OF RIBOFLAVIN TRANSPORTERS IN MOTOR NEURON DISEASES: Genetic analysis of the Brown Vialletto Van Laere and Fazio Londe syndromes and development of potential treatment strategies for motor neuron diseases.**

After careful consideration of the reviewers comments, the review panel fully agrees with the score reached in the F2F process.

GR-2010-2309474**EXACT- EXPLORING ACTIONS: A FUNCTIONAL APPROACH TO DECODE REPRESENTATION OF MOTOR ACTS IN THE HUMAN BRAIN**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.25

GR-2010-2309551**Regulation of mTor functions by Che-1**

Reviewers initially expressed discording evaluations. As a result, F2F was performed but it was reported only the summary of both reviewer comments without justification on new score. An additional review was performed. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:15.75

GR-2010-2309687**Identification of biomarkers able to predict malignant transformation of dysplastic nodules in the cirrhotic liver.**

Reviewers initially expressed discording evaluations. An additional evaluations was performed. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2309856**SAFETY AND EFFICACY OF LICENSED BONE MARROW DERIVED AND INTERFERON-gamma PRE- TREATED MESENCHYMAL STROMAL CELLS (MSCs) IN PATIENTS AFFECTED BY SEVERE, INTRACTABLE CHILDHOOD-ONSET CROHN DISEASE AND JUVENILE IDIOPATHIC ARTHRITIS. A PIVOTAL TRIAL.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:18.5

GR-2010-2309932**Prediction of cognitive impairment in Parkinsons disease: genetic, biochemical and functional neuroimaging study**

Reviewers dis agrees on scoring (4 vs 18). However, while the F2F was lacking, the reviewer code 1711451 (score 18) has much more thoughtful comments due to his/her background in fMRI. Both reviewers agrees on a final score of 13.5 which the scientific review committee found acceptable.

GR-2010-2309933**CREATION OF A BIOLOGICAL BANK AND SEARCH FOR BIOMARKERS OF DISEASE FROM THE POPULATION-BASED REGIONAL REGISTRY OF PATIENTS WITH AMYOTROPHIC LATERAL SCLEROSIS IN EMILIA ROMAGNA REGION**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2309961**Driving Neuronal Recycling in Developmental Dyslexia. Toward a Neuro-Psycho-Educational approach to differentiate rehabilitation strategies according to different neuro-functional profiles of dyslexic children.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2310057

The role of TRAP1 in the resistance to anti-EGFR1 agents in human colorectal carcinoma

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2310116

A randomized controlled trial of diet and physical activity in BRCA mutation carriers

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.0

GR-2010-2310165

Role of TIR8 in modulating ischemia/reperfusion injury in kidney transplantation

Reviewers expressed discording evaluating scores of 5 and 18. However, the scientific review committee re-evaluated the actual proposal and felt that this review should be made, specifically to address the score of reviewer code 1711323 (18). After extensive review, the Scientific Review Committee judge that proposed project is overly ambitious and overachieving. The high number of proposed studies are not feasible within the allotted time. The Scientific Review committee suggest to narrow down focus to ensure feasibility. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on final score 11.5

GR-2010-2310396

Sagittal balance in degenerative pathologies: analysis of the radiological, biomechanical and biological aspects involved in the standing position of the spine, pelvis and limbs.

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2310415

GENOTYPE AND ENVIRONMENT INFLUENCES ON THE TUMOR PROLIFERATION DYNAMICS INFERRED WITH NEXT GENERATION SEQUENCING

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2310476

Isoform-selective histone deacetylase inhibitors in experimental models of ALS: molecular and therapeutic effects

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:14.0

GR-2010-2310483

Individual Susceptibility to Plaque-Induced Periodontal Inflammation: Evaluation of Genetic, Clinical, Immunological and Microbiological Markers.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:11.5

GR-2010-2310585

Identification and evaluation of markers of malignancy in thyroid nodules with undetermined cytology

Reviewers expressed discording evaluations and an additional review was performed. Each of the three submitted reviews points out important issues concerning the application. As highlighted by reviewer code 1713045, the methodology could have been described in greater detail. To level the differences between the reviewers evaluations, the commission recommends a slightly more positive score than the mathematical average. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.5

GR-2010-2310662

FEASIBILITY AND COST-EFFECTIVENESS OF A MULTIDISCIPLINARY HOME-TELEHEALTH INTERVENTION PROGRAMME TO REDUCE FALLS AMONG ELDERLY DISCHARGED FROM HOSPITAL: A PILOT RANDOMIZED CONTROLLED TRIAL

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.5

GR-2010-2310699

Molecular investigation and clinical relevance of RET expression in breast cancer

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2310813

Molecular epidemiology, Immunoproteomic and host-parasite interaction of Echinococcus granulosus complex

Reviewers initially expressed discording evaluations. An additional review was performed. As a result, F2F was performed. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:14.75

GR-2010-2310843

Hybrid revascularisation by combined CABG and PCI in multivessel coronary disease: clinical outcomes and optimal management. An observational study.

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2310896

Anti-thrombogenic and antimicrobial intravascular catheters for patients hospitalized in clinical settings for neuromotor rehabilitation and long-term care

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.0

GR-2010-2310976

Dissecting host-parasite interactions by RNA interference knock-down of erythrocyte membrane microdomain proteins

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.25

GR-2010-2310977

Normalization of defective calcium handling in cardiac pathologies: innovative strategies and potential therapeutical applications

After having evaluated the proposal and the reviewer's comments, the committee agrees with the final score suggested by both reviewers in the face to face.

GR-2010-2311002

A scoring system to predict the risk of developing post operative atrial fibrillation

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2311080

Study of new factors associated with pathogenicity in V. parahaemolyticus and nonO1 nonO139 V. cholerae and multilocus sequence typing approach for epidemiological surveillance

Reviewers provided contrasting feedback; nevertheless, both referees carefully motivate the assigned score After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:13.25

GR-2010-2311188

Correlation between HIV Associated Neurocognitive Disorders (HAND) and HIV- and Cytomegalovirus (CMV)-specific immune activation and inflammation in peripheral blood and central nervous system (CNS) in HIV-infected antiretroviral-naive patients

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2311287

Neurofibromatosis: a spectrum of multifaceted disease

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.75

GR-2010-2311379**Study of the molecular profile of circulating tumor cells for outcome prediction to docetaxel in metastatic castration-resistant prostate cancer patients**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2311473**Immunohistochemical and miRNA analysis of tumoral neoangiogenesis in small liver lesions: diagnostic and prognostic value of old and new markers.**

The reviewers provided contrasting feedback; nevertheless, both referees carefully motivate the assigned score. An additional review was performed. The committee recognized the accomplishment the principal investigator, although weaknesses were raised regarding the overall rigor of the statistical plan. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score 15.

GR-2010-2311594**Translational research of the multi-dimensional care model "MI PIACE PIACERMI" for childhood obesity treatment in ambulatory care setting and in-patient treatment**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:18.0

GR-2010-2311854**Effects of Testosterone supplementation on clinical and rehabilitative outcomes in older men undergoing on-pump CABG**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:11.75

GR-2010-2311876**Pharmacological approaches to improve the thymic defect and prevent autoimmunity in a murine model of Omenn syndrome: therapeutic implications.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2311898**Identification of novel determinants of therapeutic response to targeted therapies and of new druggable driver oncoproteins in patient-derived xenografts from primary HER2 positive and triple negative breast cancers.**

The committee collegially reviewed the grant and acknowledged the lack of a careful revision by reviewer code 13003073 who failed to identify some critical flaws of the grant and provided a poor justification of the scores. The main concern is the lack of innovation as similar studies can be found in the literature. The PI also fails to justify how the study would differ from other current research and does not address the issue of statistical analysis and of representativeness and relevance of his findings. In the F2F phase the 2 reviewers failed to really discuss the project and to justify their agreement. Considering that in the F2F the comments of the reviewer that assigned the higher score have been maintained and not changed by the reviewer that assigned the higher score, who failed to improve the overall comments on the grant. The committee aligned its evaluation to the one of the more critical and better articulated comments of the reviewer code 171113 and assign the final score of 10 to the proposal.

GR-2010-2312023**MEF promotes stemness in the pathogenesis of gliomas**

Both reviewers provided very positive and encouraging comments, yet slightly negative scores that do not match their notes. The committee greatly appreciated the study design the innovation and the relevance. The feasibility of the whole grant also needs to be praised as the description of the methodology is very accurate and clear. The only concern is about the skills of the applicant who doesnt have a very strong publication record. Close mentoring is recommended. In view of the strengths and potential impact of the study, the committee agrees on the score of 8.5

GR-2010-2312025**A health technology life cycle model from emerging to obsolete technologies**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312034**The endocannabinoid system as target in colon cancer and associated cachexia**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312060**Expression profile and risk haplotypes identification in peripheral blood of stroke patients with carotid atherosclerotic plaques**

The reviewers provided similar feedbacks. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:10.0

GR-2010-2312082**IR-A as a new player of sarcoma malignancy**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312121**A NEW STRATEGY FOR A HIGH PREVALENCE CONDITION: ORTHOSTATIC HYPOTENSION. WHATS UP IN REHABILITATION SETTING?**

Reviewers initially expressed discording evaluations. An additional evaluations was performed. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on final score 14.5

GR-2010-2312185**Pancreatic non-endocrine fraction conversion into insulin producing tissue by acting on TLRs: a potential pathway to improve the transplantable beta-cell mass for T1DM therapy**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312208**NEW BIOMARKERS FOR THE EVALUATION OF SPERM DNA STATUS IN ONCOLOGICAL PATIENTS.**

The reviewers provided contrasting feedback; and both referees carefully motivate the assigned score. The committee recognized the accomplishment the principal investigator, although some weaknesses were raised, specifically a lack of appropriate statistical analysis plan and unclear clinical translation/impact. On these premises, the review scientific committee agrees on the average as final score:13.5

GR-2010-2312299**New recreational drugs of abuse intoxication: prevalence estimation in the Emergency Departments referring to the Pavia Poison Centre**

Reviewers initially expressed discording evaluations. As a result, F2F was performed but it wasn't well documented. The scientific review committee agrees to perform a new evaluation.

Scientific quality and relevance of the research Text: The epidemiology of new designer drugs is of interest and relevant to the public health system. The application will study patients accessing the poison center, and proposed studies will screen for cases of new drugs abuse. Score: 3

Innovation and originality of the project (relative to the current international literature). Text: The project is quite innovative since data are not available. A network or database including detailed information about emergency departments patients would be a first step to described and characterized the at risk population. Applicant should describe available international literature on the same topic; so that a comparison can be made to other European countries in order to predict outcome. Score: 5

Methodology and development strategy of the project (over its three-year duration), preliminary data and bibliographical reference Text: The methodology is based upon open enrollment of patients accessing the ER or Poison Center. However, the application includes preliminary data suggesting feasibility and experience with similar clinical and epidemiological studies. A weakness is that the PI does not describe

the analytical chemistry methods employed. For instance, how do they intend to detect novel designer drugs? It is not clear what analytical chemistry core capabilities are available to conduct the study. It is not clear how informed consent will be obtained from intoxicated patients. It is not clear how data will be analyzed after being collected. Since the recruitment is open, is it possible to predict how many patients will be admitted to ER within a given time, in order to estimate sample availability? Score: 6
Profile of the Investigator and his/her scientific work Text: The background is appropriate Score: 3
The scientific review committee agrees on final score:17

GR-2010-2312339

Role of DNA methylation in diagnosis and prognosis of prostate cancer.

The two reviewers have provided thorough descriptions of the project of its relevance, strengths and weaknesses. They also started, but don't complete, the F2F process and proposed to give to the project the average 9.5 of their 2 evaluations. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:9.

GR-2010-2312367

Familial hyperlipidemias: new diagnostic approaches

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:16.25

GR-2010-2312416

Development of cytochrome c assay marker of ischemia/reperfusion damage to the heart

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:14.0

GR-2010-2312522

Amyotrophic lateral sclerosis (ALS) swine models: production and characterization

After having evaluated the project and considered the reviewers comments, the review panel committee agrees on the average as final score: 6.25

GR-2010-2312562

Molecular characterization of the Apical Membrane Antigen-1 from Italian strains of Babesia bigemina and study of its role in the protective host immune response.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:14.25

GR-2010-2312568

A WEB based, paperless and open source implementation of IHE radiological and nuclear medicine workflow

Fair Review. The score of the F2F is confirmed.

GR-2010-2312570

Toward a molecular criterium for the diagnosis of multiple Sclerosis. A proteomic and redox proteomic study

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312592

Studying Down Syndrome allows to early diagnose Alzheimers disease

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312614

Predictive biomarkers of dementia: a longitudinal evaluation of Mild Cognitive Impairment

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312621**An innovative machine perfusion (Bologna machine perfusion) for abdominal organs preservation before transplantation. Optimization of perfusion, temperature and oxygenation-related variables.**

Reviewers expressed discording evaluations. An additional review was performed. The project is relevant, the PI and team is excellent. The methodology: the methods are general the timeline is appropriate for an experimental device development, that to say they are planning to put together the project once they have the funds or better understanding (vague). They are planning to use the device after animal model to be used in humans that is arbitrary. The molecule biology component comes out in the model suddenly. I believe there is a major conflict of interest with the companies that have interest with the methodology and device development. It should be better investigated. Scientifically the reviewer with score 15 has legitimate concerns. The 3rd reviewer also gave a 10. The committee may also raise place a concern to remove the study because of conflict of interest (companies involved in the study design and development). After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:9.75

GR-2010-2312630**Flexible endoscope used in laparoscopic surgery: analysis of possible applications**

Valid proposal with some concerns in the methodology. In specific the study lacks a comparison group, lacks preliminary data to justify the number of subjects involved, After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:12

GR-2010-2312652**Leptin, metabolic state and natural regulatory T cells: cellular and molecular basis for a novel immune intervention in multiple sclerosis**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312686**Nanostructured Coatings Enhancing Material Performances in Joint Arthroplasty**

After having evaluated the project and considered the reviewer comments, the review panel committee agrees on final score:8

GR-2010-2312693**Role of HMGB1 redox state in cardiac tissue regeneration and cardiac progenitor cell function**

The reviewers provided contrasting feedback; nevertheless, both referees motivate the assigned score appropriately. An additional review was performed. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on final score: 6.5.

GR-2010-2312702**Next generation sequencing to speed up molecular diagnosis and to identify novel causes of hemolytic uremic syndrome**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312713**Role of PI3K-beta in cardiac remodeling and failure**

Reviewers showed a disagreement on evaluation providing a score of 5 and 18.5. Reviewer code 1760242 (18.5) noted that the hypothesis that PI3K-beta may be involved in the pathophysiology of cardiac remodeling and failure is original. However, this possibility is not sufficiently supported by preliminary data. Importantly, the large number of studies and the use of three transgenic mice combined with three cardiac failure models, question the feasibility of the experimental design together with the interpretation of results to be obtained. Reviewer 13003156 (5) noted that there are no information about clinical relevance of PI3Kbeta in cardiac stress, remodeling and failure; and that there are not clearly visible milestones and limitations. The Scientific Review Committee agrees that the proposed studies are overly ambitious and should be narrowed down in order to show feasibility. Too many mouse in vivo studies are proposed within the allotted time, including cardiac models which are quite complex. The committee agrees the F2F final score: 11.5

GR-2010-2312768

Endoscopic treatment of obesity and type 2 diabetes by endoluminal device (Endobarrier): a prospective study

Reviewers expressed discording evaluations. The scientific review committee agrees on perform a new evaluation

Innovation: Endoscopic treatments of obesity have not been shown to be effective in maintaining long term BMI reduction and diabetes remission. A new endoscopic approach is need, nevertheless it has been shown recently that bariatric surgery is the most effective treatment in patients with obesity/diabetes. Score 4

Profile of the investigator: The PI is MD with experience mainly in pancreatic diseases. The PI does not have any publications in the field of obesity and bariatric surgery and lacks also a PhD/Doctorate title. No high impact factor publications. Score 7

Scientific Quality and Relevance of the research: This study aims to confirm in an Italian population, a study published in 2010 in an European court. It has been shown in 2 studies published in April 2012 in the New England Journal of Medicine that the most effective treatment for obesity/diabetes is represented by bariatric surgery. In this view, any proposed new therapeutic approach should be compared with bariatric surgery. Score 6

Methodology: The study design is very poor. There is no control group in particular results obtained with Endobarrier should be compared with the other therapeutic approaches that have been shown to effective in reducing the BMI and inducing remission of diabetes. Moreover, a correct stratification of the patients should be planned according to comorbidities that could affect the outcome. Score 8

Final: The proposal is from an investigator with no experience in obesity/bariatric surgery. The study wants to confirm in an Italian population, a previous published study made in European patients. The design is not proper since there is no comparison group. The review panel committee agrees on final score:25

GR-2010-2312769

DESIGNING MOLECULAR CHAPERONS FOR PROTEINS: A NEW STRATEGY FOR DRUG DISCOVERY IN NEURODEGENERATIVE DISEASES

A well articulated proposal supported by encouraging and strong preliminary data and a strong team. After attentive re-exam, the committee confirms the reviewers scores resulting from face-to-face assessment.

GR-2010-2312796

THE ROLE OF MELANOPsin RETINAL GANGLION CELLS IN PHOTOENTRAINMENT OF CIRCADIAN RHYTHMS IN NEURODEGENERATION AND AGING

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312852

PROMOZIONE DELLA SALUTE ORALE NELLE REALTA SCOLASTICHE DELLA ASL MILANO

Reviewers initially expressed discording evaluations. As a result, F2F was performed. The scientific review committee agrees on F2F final score

GR-2010-2312855

Deciphering the genetic complexity of myeloproliferative neoplasms and the molecular pathways involved in disease progression

Reviewers initially expressed discording evaluations . An additional review was performed. The committee recognized the accomplishment the principal investigator, although was noted that the most part of the project will be carry out in an external lab. Numerous weaknesses were raised with an unclear sample size, lack of a realistic power assessment with regard to the numbers of subjects and a vague description of the statistical analysis plan. The study seems overly ambitious. The committee confirmed the score 9.0.

GR-2010-2312866**An intervention aimed at improving the cognitive, physical, and psychiatric functioning of patients with Mild Cognitive Impairment: A randomized control trial of physical exercise and cognitive stimulation.**

Reviewers initially expressed discording evaluations . An additional review was performed. The proposed work has high clinical relevance and the committee recognized the accomplishment the principal investigator, although the lack of preliminary data was noted. 500 hundreds are patients are too many to be reasonably feasible (the number of patients examined each year during regular clinical activity is not provided). The number of required patients could be reduced by combining exercise and cognitive therapy (otherwise, 3 outcomes are too many, and it would be expected that the best clinical results would be obtained by combining physical activity and cognitive stimulation. The study might also be improved by adding psychiatric evaluation by a board-certified psychiatrist. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on final score:9.8

GR-2010-2312893**The role of the cerebellum in emotion recognition processes: cerebellar TMS as a rehabilitative treatment for schizophrenic patients.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2312924**Neuroinflammation and synaptic function: an electrophysiological analysis in experimental multiple sclerosis**

After having evaluated the project and considered the reviewers comments, the review panel committee confirmed the score assigned during the F2F

GR-2010-2312952**PKC beta as new target to prevent pharmacologically induced weight gain during antipsychotic treatment.**

A good proposal by a well accomplished investigator. After attentive re-exam, the committee confirms the reviewers scores resulting from F2F assessment

GR-2010-2313020**Exploring the effects of different intensity and frequency of robotic gait training in patients affected by a severe stroke in subacute phase**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2313064**Pathogenetic role of B cell-activating factor and novel markers of lymphoma onset in Sjögren's syndrome**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.0

GR-2010-2313085**NANOSTRUCTURED SCAFFOLD TO ENHANCE NERVE REGENERATION**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2313099**Topoisomerase I from Leishmania infantum as potential chemotherapeutic target**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2313255**Integration of advanced molecular analyses and magnetic resonance imaging for the identification of biomarkers of disease progression in multiple sclerosis.**

The committee has re-evaluated the project and the score given by the two reviewers during the F2F discussion is collegially confirmed. This is an important proposal that could contribute significantly to the identification of biomarkers of MS progression, possibly improving the ability of the health services to establish more targeted early treatment plans in MS patients. The proposal is in line with the priorities set forth by the Italian Ministry of Health and the given score is appropriate.

GR-2010-2313261**Health impact assessment and health care costs of respiratory tract infections (RTI) in general population and hospitalized patients in Palermo (Western-Sicily).**

Reviewers expressed discording evaluations and an additional review was performed. The average score of the first two reviewers score is 12.25. A third revision gave a low score of 7.5. The concerns of the reviewer code 1717275 are valid and substantial. The study fails to address reliable hypothesis with a clear cut aims. It seems more an investigational expedition with a shotgun approach. It is not clear also whether the study timeline will be completed in the 3 years time period of funding. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:12.25

GR-2010-2313329**Analysis of HCV persistence in the host and its implications in virus-related lymphomagenesis**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.75

GR-2010-2313416**Characterization of bone marrow endothelial cells in patients with chronic myeloproliferative diseases: towards anti angiogenic therapy**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:14.25

GR-2010-2313474**GENETIC SUSCEPTIBILITY AND PHARMACOGENETICS OF MULTIPLE MYELOMA AND MGUS**

A good proposal by a well accomplished investigator. After attentive re-exam, the committee confirms the reviewers scores resulting from F2F assessment.

GR-2010-2313580**Non invasive brain stimulations: EEG reactivity in vegetative and minimal conscious state patients**

Reviewers expressed discording evaluations and an additional review was performed. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:16.25

GR-2010-2313613**Analysis of serotype, virulence-factor diversity and antibiotic resistance pattern of E. coli strains isolated from ruminant and human samples in Sicily.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:20.25

GR-2010-2313719**Development of a carbon nanotube DNA biosensor for rapid detection of subgingival microbiota involved in periodontal diseases.**

Reviewers expressed discording evaluations and an additional review was performed. The PI has no real expertise in the field of nanomaterials and therefore the feasibility of the project is seriously questionable. Even if the clinical area is of interest and the impact of the research significant, preliminary data showing the ability of the PI to conduct the research are not exhaustive. Also his co-PIs have no established record of previous publications in the area of carbon nanotubes synthesis and functionalization. The reviewers provided contrasting feedbacks and on these premises, the reviewers committee proposed as final score 15.

GR-2010-2313731**Investigating the role of heterochromatin destabilization and Rif1 in the Italian breast cancer population**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:13.25

GR-2010-2313798**Genetic basis of steroid resistant nephrotic syndrome and implications for therapy**

Reviewers expressed discording evaluations and an additional review was performed. Project aimed to investigate genetic determinants involved in steroid resistant nephrotic syndrome. The profile of the PI is weak given that he has a total of only 4 publications although a New England's one. The only concern regarding the study design, sits in the control group that should be defined better according to precise inclusion and exclusion criteria. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:11.5

GR-2010-2313990**Identification of microRNAs as novel therapeutic targets and biomarkers for the advancement of anti-cancer strategies of human hepatocellular carcinoma**

Reviewers expressed discording evaluations and F2F wasn't well documented. The committee has re-evaluated the project and its assessments. This research project, presented by a young investigator, aims to investigate the role of microRNA in the pathogenesis of hepatocellular carcinoma. The committee agrees that this idea applied in animal models lacks originality. Indeed, a paper has recently been published in Hepatology (Callegari E, Hepatology April 2, 2012) showing that microRNA-221 promotes liver carcinogenesis in mice. Furthermore, in such recent publication the PI of this proposal submitted to the Ministry of Health has position number 6 among the authors. This element raises a concern regarding the originality of the idea. Moreover, the methodology should be carefully improved. In particular the number of patients and controls, the recruitments plans, the inclusion and exclusion criteria should be precisely defined. To be considered also that hepatocellular carcinogenesis has a multifactorial etiology (liver cirrhosis, HBV, HCV, NASH..) therefore, an accurate analysis in which patients are stratificated according to the etiology should be performed. In this view, the committee decides that the final score is the average of the scores of the 2 reviewers, i.e. 10. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:10

GR-2010-2313997**Large-Scale Maladaptive Neuroplasticity in Chronic Migraine: Implications for Novel Neurophysiological Treatments**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2314052**Transthyretin (TTR) amyloidosis: modulation of amyloidogenesis and neurotoxicity of three TTR variants.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.5

GR-2010-2314189**Generation of protective immune regulatory environment in murine models of Multiple Sclerosis by CTLA4- Ig-mediated tryptophan catabolism.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2314242**Biomolecular profiling of cutaneous squamous cell carcinoma and precursor lesions: HPV infection, immune system genes expression and polymorphism, miRNA analysis and novel biomarkers investigation**

Reviewers expressed discording evaluations and two additional evaluation were performed. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:15.25

GR-2010-2314368

POTENTIAL ROLE OF INFLAMMASOME AS INTRACELLULAR MEDIATOR OF INFLAMMATORY MANIFESTATIONS IN GAUCHER DISEASE (GD)

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2314478

Non-invasive cerebral PET data quantification with aortic image-derived input function

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:14.0

GR-2010-2314518

SENSITIZING GLIOBLASTOMA CELLS TO CHEMOTHERAPY BY PRO-DIFFERENTIATING AGENTS

Both reviewers provided very positive and encouraging comments, yet slightly different scores. The reviewers evaluated differently the study design and feasibility, as well as the skills of the applicant; however, they agree that the project is of great clinical relevance. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.75

GR-2010-2314529

MOLECULAR PROFILING OF HEPARAN SULFATES IN M.O. PATIENTS: EVALUATION OF PATHOPHYSIOLOGICAL PATHWAYS TO DEFINE A COMPLETE BIOCHEMICAL PROFILING FOR DIAGNOSIS AND PATIENTS FOLLOW-UP.

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2314561

Nanosize imaging with brain amyloid/tau targeted nanoparticles as an in vivo biomarker for Alzheimers disease pathology

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2314575

Diagnosis of attention-deficit/hyperactivity disorder (ADHD) in adults by quantitative EEG and transcranial magnetic stimulation markers.

The committee has re-evaluated the project and the score given by the two reviewers during the F2F discussion is collegially confirmed. This is an important proposal that could contribute significantly to the identification of supporting diagnostic elements in ADHD patients. The proposal is in line with the priorities set forth by the Italian Ministry of Health and the given score is appropriate. The scientific review committee agrees on F2F final score

GR-2010-2314687

Comparative effectiveness of AVR and TAVI procedures for severe symptomatic aortic stenosis treatment: results from the real world

After careful evaluation, and in consideration of the very high quality of the PI who submitted requests in this call, the review panel disagrees with reviewers evaluation of the PI profile; the PI scientific production is certainly good, she published about 20 papers in nine years. However, most of her production is on small, national journals, as also highlighted by a rather low-h-index. The review panel therefore amends the score to 4, which brings the final score to 10, to balance the evaluation in respect to other proposals examined in the study section. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:10

GR-2010-2314703

Role of Nuclear Receptor Coactivator PGC1-beta in the Intestinal Epithelium

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:5.25

GR-2010-2314886

The ASAA study. Antibiotics vs. Surgery in Acute Appendicitis: an intention to treat prospective randomized controlled study

Reviewers initially expressed discording evaluations. An additional evaluations was performed. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2314935

Disorders of consciousness: longitudinal Italian study on Vegetative State and Minimally Conscious State (ITADOCs)

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2314957

Adipose tissue remodelling from white to brown phenotype as preventive treatment for type 2 diabetes and as potential tool to protect against metabolic diseases of aging.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.75

GR-2010-2314998

Strategies to improve functional recovery in presence of cerebellar pathology

Reviewers initially expressed discording evaluations. An additional evaluations was performed During the face to face appeared to be a consensus for a rated 14 because of issues with methodology. A third reviewer agrees on the quality of the proposal but assigning a rating of 6. The design does not appear to be robust enough. It is not clear whether the environmental manipulation proposed will make a difference in the plasticity After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:12.5

GR-2010-2315007

Striatal cholinergic interneurons as a novel target for the treatment of Parkinson's disease

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented In reference of the current project, GR-2010-2315007, the committee, based on the referee's comments 13003080 has accepted the value of 8. The cited referee has indeed confirmed that the original credited values were initially inverted. According to the Face to Face the mistake has been recognized. The scientific review committee agrees on F2F final score

GR-2010-2315120

Platelet activation in type 2 diabetic patients with stable Coronary Artery Disease: insights into their thrombotic propensity using a Genome-Wide approach.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.0

GR-2010-2315177

New tools to identify effective SMA therapeutics: a protein-fragment complementation assay coupled to snRNP biogenesis to measure the SMN complex activity in SMA cells

A good proposal by a well accomplished investigator. After attentive re-exam, the committee confirms the reviewers scores resulting from F2F assessment.

GR-2010-2315201

Pathogenicity, virulence and antibiotic resistance mechanisms of Multi-Drug-Resistant (MDR) Gram- negative bacteria: impact on Rehabilitation Facility patients and on infection control strategies.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:24.5

GR-2010-2315208**PRIMARY CILIUM, NPC1 AND PATCHED1 PROTEINS, AND CERAMIDE IN NIEMANN-PICK TYPE C DISEASE**

The reviewers provided contrasting feedback. The review scientific committee concur with the lower score given by reviewer code 1300300. This is justified by the PI modest publication record (no first author publication among the 5 best publications and only 1 first author publication listed in the 5 most recent publications) and the limited novelty of the research approach. The PI, in fact, proposes to verify possible structural and morphological alterations of primary cilia in cultured fibroblasts of NPC1 patients. However, fibroblasts are well known to quickly re-differentiate in vitro, so it is unclear how cultured fibroblasts extracted from skin biopsies will reflect real pathological fibroblasts. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:10.5

GR-2010-2315375**Development and therapeutic potential evaluation of L-glutamate and kynurenic acid analogues in an animal model of meningococcal meningitis.**

Valid research proposal. After careful review of the proposal the review panel committee agrees on the higher value assigned by one of the reviewers because balance the lack of direct translational application and balance the overall quality. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:10

GR-2010-2315454**Genetic analysis of TPH2 in patients with Major Depression as a predictor of SSRI responsiveness.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2315619**New potential targets for reverting diabetic dysfunction in progenitor cells mobilization and homing**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2315721**Molecular and in vivo analysis of in vitro generated cancer stem cell-like cells: identification of pathways involved in CSC generation and maintenance**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2315743**A training for dementia family caregivers to improve resilience and well-being: a Sicilian perspective.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:19.5

GR-2010-2315765**Targeting Th17 in cystic fibrosis as a pharmacological strategy and immunogenetic screening**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2315767**Rising up brain activity by non invasive brain stimulation to improve cognitive and behavioural abilities in patients with Alzheimers disease**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2315848**Randomized Controlled Trial of Ultrasound enhanced thrombolysis in acute anterior circulation stroke**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2315918**Sleepiness related accident risk in sleep disorders with excessive daytime sleepiness: from driving simulator performance to real road accident risk.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2315997**Virus evolution and virus-host interaction in the pathogenesis of severe influenza virus A infections**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:13.0

GR-2010-2316044**NON INVASIVE BRAIN STIMULATION AS ADJUVANT THERAPY FOR ALZHEIMER DISEASE**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.75

GR-2010-2316125**Involvement of dysregulated OPG/RANK/RANKL axis in atherogenesis and acute coronary syndromes**

The reviewers provided contrasting feedback; nevertheless, both referees motivate the assigned score appropriately. An additional review was performed and F2F didn't solve some concerns. On these premises, the commission perform a new evaluation reported follow.

Scientific quality and relevance of the research: The present project may contribute to better understand of the role of dysregulated OPG/RANK/RANKL system during acute coronary syndromes and atherosclerosis progression. Score : 1.5

Innovation and originality of the project (relative to the current international literature): To the reviewer's knowledge the role of dysregulated OPG/RANK/RANKL system during acute coronary syndromes and atherosclerosis has not been described so far. Score : 1.5

Methodology and development strategy of the project preliminary data and bibliographical reference

Text: The PI doesn't describe his role in this project. Moreover, in aim1 there is no statistical justification of the number of patients included in the study and no information about how confounding variable will be evaluated (like gender, ethnicity). The in vitro experiments are not well described. Score : 7

Profile of the Investigator and his/her scientific work: The principal investigator has a good number of publications in the field of atherosclerosis and vascular calcification. Score : 3

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:13.0

GR-2010-2316138**INNOVATIVE METHOD FOR THE TREATMENT OF TOTAL LIMBAL STEM CELLS DEFICIENCY (LSCD) THROUGH A TISSUE-ENGINEERED HEMICORNEA**

Both reviewers provided very positive and encouraging comments, yet slightly negative scores that do not match their notes. The committee greatly appreciated the study design the innovation and relevance. The full feasibility of the whole grant is the only partial concern and might require a revision of the budget to exclude phase II. The skills of the applicants team reassure the committee that agrees that the project is of great clinical relevance and the committee endorses funding. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the F2F final score:8.5

GR-2010-2316169**Dissecting the molecular bases and clinical variability of familial Alzheimer's disease**

The idea behind the project is valid; nevertheless, major concerns cast shadow over this application.

The project proposes very complex genomics analyses, which include miRNA profiling, methylation studies, and exome sequencing. The applicants background is in genetics, yet her track record fails to demonstrate she has the skills required to handle such demanding genomic approach. The methods are challenging and laborious, and it is unrealistic to believe that the applicant will complete the study in the designed time frame because. The applicants lack of experience in high-throughput genomics is also evidenced by the absence of bioinformaticians. It is unclear how the applicant plans to analyze the enormous amount that a project as the submitted one might generate. Data analysis represents in fact a major challenge and is at least naïve to believe that it can be accomplished in the last two months of the project, as planned by the applicant. It should be also stressed that similar studies are already ongoing in large international consortia involving hundreds, if not thousand, of cases; the proposed project is

based on a modest cohort and is therefore unclear which contribution it might provide. Did the applicant double-check that the size of the cohorts will guarantee sufficient statistical power to reach statistical significance? In the past years, GWAS have clearly shown that high background noise represents a major problem in this kind of analysis. The applicants CV and track record is good; yet, she might need additional experience and publication to develop the skills required to coordinate a genomic project on a large cohort of patients. The review scientific committee agrees on the final score 12.5

GR-2010-2316252

Validation of an event-based progression model of Alzheimer disease incorporating quantitative MRI information

No definition of MT. Italian name but PI is not currently resident in Italy, and holds a Chair position in England. The sketch contributor is also resident abroad. The authors state that the aim to identify a number of key events which characterize AD pathology from the earliest stages. This is not supported by the methods as they do not intend to recruit AD patients based on clinical severity. Overall feasibility appears low. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:10.5

GR-2010-2316306

Prediction of patient-specific total knee arthroplasty outputs: development of a validated patient-specific numerical tool to predict contact mechanics and polyethylene stress

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.25

GR-2010-2316308

Why are MSCs therapeutic?

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2316359

Longitudinal clinical-neuropsychological study of subjective memory complaints

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the F2F final score:9.25

GR-2010-2316474

Microbiological hazards in ready-to-eat fruit commodities

Despite the first reviewer carefully motivates the assigned score, unfortunately the PI publication record is inexistent After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:12.0

GR-2010-2316475

Alteration in cortical parvalbuminergic System in murine model of Huntingtons Disease: Pharmacological effect of Phosphodiesterase type 4 (PDE4) inhibition.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:7.75

GR-2010-2316513

Exploring hierarchical immunogenicity of mismatched HLA haplotypes for the design of innovative functional matching algorithms in allogeneic transplantation

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2316539

Neurophysiological markers of neuroplasticity in normal and pathological aging

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2316541

Risk assessment of arsenic exposure from rice-based food in children with celiac disease. Study of urinary metabolic profiles and genetic polymorphisms.

Reviewers expressed discording evaluations After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.0

GR-2010-2316561**SURVIVE: Chemokines as new therapeutic drugs for cell viability and functional recovery in brain ischemia.**

The reviewers disagree on the evaluation of this project (13.5 vs 5). One of the reviewers code 1710967 (13.5) noted that the approach is rather unclear and overly ambitious, seeking to use numerous knockin and knockout mice. There are also concerns about the CNS permeability of chemokines administered systemically. The reviewer committee reviewed the proposed studies and found that the project, albeit interesting and innovative, is too ambitious and broad in scope. Aims should be narrowed down to justified feasibility within the allotted time. In particular, it does not seem realistic to conduct all proposed brain slices electrophysiological recordings from KO mice, simply due to breeding timelines and sampling rate (brain slice recording e-phys). The Scientific review committee agrees with reviewer code 1710967 (13.5) since reviewer code 13003097 (5) did not properly address critical aspects of the proposal. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:13.5

GR-2010-2316594**DEVELOPMENT OF A MULTIFUNCTION PLATFORM FOR TELEREHABILITATION**

The reviewers provided contrasting feedback, and both referees motivate the assigned score appropriately. An additional review was performed. It is alarming that the PI has never published a first-author publication, which raises concerns his ability to carry out the work and it greatly diminishes the overall feasibility of this project. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on final score:14.5

GR-2010-2316671**Functional and structural changes induced by repetitive transcranial magnetic stimulation on corticostriatal pathway in models of Parkinsons disease and dyskinesia**

The committee has re-evaluated the project and the score given by the two reviewers during F2F discussion is collegially confirmed. This is an important proposal that could contribute significantly, although not immediately/directly, to a refined clinical use of rTMS in patients with Parkinsons Disease. The proposal is in line with the priorities set forth by the Italian Ministry of Health and the given score is appropriate. The review scientific committee agrees on F2F final score: 8.5

GR-2010-2316738**Programmed cell death and the cross-talk between the NF- κ B and the HIF signaling pathways: implications in hypoxia/ischemia-associated brain injury**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:18.75

GR-2010-2316745**SPES Service for detection of Pre-psychoses: from gene-environment interactions to phenomenology**

The committee confirms the score attributed by the two reviewers during the F2F discussion. The potential translational impact of the project is relevant. However, there are two methodological concerns that the committee would submit to the investigators: 1) a more focused, less ambitious and more hypotheses-driven project would have reassured the committee about the feasibility of the proposal; 2) the methods to study gene-environment interactions could have been described in greater detail, especially since the proposal has mixed methods in terms of both quantitative genetics (twin-study) as well as molecular genetics, and the interplay between such different areas of research are not described in detail.

GR-2010-2316749**Role of dual purinergic/cysteinyl-leukotrienes receptor GPR17 in inflammatory conversion of cardiac resident progenitors following myocardial ischemia**

Reviewers initially expressed discordant evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2316776**A machine-learning approach to pharmacogenomics. Application to therapy of autoimmune diseases, Myasthenia Gravis and Multiple Sclerosis.**

The committee has re-evaluated the project and the score given by the two reviewers during the F2F discussion is collegially confirmed. This is an important proposal that could contribute significantly to the improved clinical ability to predict efficacy and tolerability of available immunosuppressive drugs in the treatment of autoimmune diseases such as myasthenia gravis or multiple sclerosis. The proposal is in line with the priorities set forth by the Italian Ministry of Health and the given score is appropriate.

GR-2010-2316798**DNA REPAIR SYSTEM AND CISPLATIN RESISTANCE IN OSTEOGENIC BONE TUMOURS: VALIDATION OF MOLECULAR TARGETS AND CLINICAL APPLICATIONS**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2316832**HIGH FIELD-STRENGTH MR SCANNERS (3 TESLA) TO DETECT BIOMARKERS FOR EVALUATING DRUG-RESISTANCE IN TEMPORAL LOBE EPILEPSY**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:23.75

GR-2010-2316862**Activation of innate host defense mechanisms in multiple sclerosis: analysis of potential involvement of Toll-Like Receptor (TLR)4, TLR9 and MyD88 adaptor using novel immunomodulatory compounds**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:23.5

GR-2010-2316918**Improving Quality of Life of Dialysis Patients. A Randomized Clinical Trial with a Psychological Intervention**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:18.0

GR-2010-2316967**CHARGE SYNDROME: UNRAVELLING THE MOLECULAR BASES WITH TRADITIONAL AND INNOVATIVE APPROACHES**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317012**Arbovirus infections in humans and vectors: potential for local outbreaks in Northern Italy**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.5

GR-2010-2317098**Targeting 14-3-3 protein to develop novel anti-parasitic drugs: the Giardia model**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:13.5

GR-2010-2317133**Systematic review on the interventions to reduce waiting lists for elective procedures**

After having evaluated the proposal and the reviewer's comments, the committee agrees with the final score suggested by both reviewers in the face to face.

GR-2010-2317162**Persistence and adaptation mechanisms of clinical methicillin-resistant Staphylococcus aureus clones**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:15.5

GR-2010-2317213**From observation to action in dementia prevention to identify prognostic and intervention monitoring tools based on non-invasive multi-markers phenotypes**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317225**Relationship between iron metabolism and proteasome functionality suggests novel therapeutic strategies for Multiple Myeloma**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317318**A molecular approach to endometriosis: towards the prediction of the response to hormonal therapy.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:19.25

GR-2010-2317339**PLASMA EXOSOMES IN THE DIAGNOSIS OF NEURODEGENERATIVE DISEASES: MiRNA SEQUENCING AND PROTEOMICS**

Each of the submitted reviews points out important issues concerning the application. The research plan is overambitious; it is unlikely the applicant will be able to complete the proposed research within the three-year period. The criteria that will be applied to select the patients are rather elusive. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.5.

GR-2010-2317413**microRNAs as early biomarkers of anthracyclines induced cardiotoxicity**

Reviewers initially expressed discording evaluations. An additional evaluations was performed. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317446**PLERIXAFOR MOBILIZED HEMATOPOIETIC STEM CELLS: AN ALTERNATIVE STEM CELL SOURCE FOR GENE THERAPY OF BETA-THALASSEMIA**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317510**Dermatological complications from metals and metal oxide nanoparticles (MONp) contained in tattoos: a population-based study**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317550**Investigating KAP1-mediated epigenetic control of differentiation and function of adaptive immune system**

The evaluations are sound and the review panel accepts the score reached in the F2F phase. Nevertheless, it should be noted that the reviewers assessments are very generous. For instances, in the investigators profile section, scores are very high and comments are glowing (e.g. impressive collection of publication). The PubMed record indicated that the applicant published 9 articles in about 10 years. The manuscripts are on good Journals and are highly cited; however, a more realistic assessment would qualify this profile as very good one, rather than impressive. The scientific review committee agrees on F2F final score

GR-2010-2317557**Safety profile and prescribing pattern of psychotropic medications in childhood.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317577**Thyroid hormones, brain tumours and macrophages**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317593**Role of the meniscus in OA pathology and symptoms**

Comments of the reviewers are appropriate. The scientific review committee agrees on F2F final score.

GR-2010-2317696**Repeated influenza A infections as a risk factor for the development of Parkinsons disease during aging**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:13.0

GR-2010-2317740**ENHANCING ISLET TRANSPLANT SUCCESFULL BY DE NOVO TISSUE EXPRESSION OF TRUNCATED ERYTHROPOIETIN RECEPTOR.**

Reviewers expressed discording evaluations A third evaluation gave even further low score because of lack of preliminary data. The proposal has some innovative and interesting aspects. The lack of preliminary data to substantiate the hypothesis are critical, besides so not significant as proposed by the 3rd reviewer After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:12

GR-2010-2317798**The neurobiology of social perception deficits in Autism Spectrum Disorders: simulation, integration and connectivity**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317863**Epigenetic remodeling of ncx1 gene by drugs inhibiting histone deacetylases (HDACs) class I: a new strategy to reduce the neuronal damage in brain ischemia**

The review panel fully agrees with the score reached in the F2F process; the reviewers carried out careful discussion before reaching an agreement.

GR-2010-2317873**Supporting an early autism spectrum disorders diagnosis through the support vector machine approach**

The committee has re-evaluated the project and the score given by the two reviewers during the F2F discussion is collegially confirmed.

GR-2010-2317900**Role of endocannabinoids in multiple sclerosis**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317953**Evidence of preclinical Alzheimers disease in healthy middle-aged persons**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:17.5

GR-2010-2317958**Population study of disability health and ageing in Lombardia (DISHAL)**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2317971**Does timing of VT ablation affect prognosis in patients VT with an implantable cardioverter-defibrillator?**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318089**Molecular mechanisms involved in HIV-related atherosclerosis: role of pathogen associated molecular patterns, type I interferons, and HIV replication.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:15.0

GR-2010-2318116**Next generation sequencing technologies applied to mantle cell lymphoma: a tool to understand its pathogenesis and to identify novel biomarkers and therapeutic approaches**

After having evaluated the proposal and the reviewer's comments, the committee agrees with the final score suggested by both reviewers in the face to face.

GR-2010-2318130**Branched peptides as novel tumor-targeting agents**

Reviewers initially expressed discording evaluations. Also two additional evaluations expressed discording score. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score: 14.5

GR-2010-2318142**Predictive role of von Willebrand Factor changes in bleeding complication during continuous flow left ventricular assist device support**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:16.75

GR-2010-2318279**High Obesity risk in Children and Adults with Narcolepsy-Cataplexy**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318338**Isolation and characterization of ependymal-derived stem/progenitor cells (epSPCs): a new in vitro model to address pathogenesis and treatment of motor neuron diseases.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318382**Assessing human minor histocompatibility antigen (mHa) and human Cytomegalovirus (CMV) specific T- cell responses as prognostic marker for infection and chronic allograft rejection.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:10.75

GR-2010-2318463**The ADP receptor P2Y13 in the regulation of megakaryocytes development in myeloproliferative neoplasms**

Reviewers expressed discording evaluations The extra evaluation recognized value to the proposal (10), however some of the concerns were appropriate. It is recognized by different reviews that it is not clear how this research will overcome potential difficulties based on the novelty of the project, in particular for the investigator. the review scientific committee approve a final score of 12.5

GR-2010-2318507**Mechanisms and treatment of Alzheimer disease: what can we learn from epilepsy?**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:14.75

GR-2010-2318511**BRAIN [18F]FDG PET NORMATIVE DATABASE**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:10.75

GR-2010-2318535**Sleep and cardiovascular disturbances as biomarkers of dementia**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:18.75

GR-2010-2318568**Analysis of myocardial function after aortic valve replacement with a novel sutureless valve: coupling mathematical models to clinical research.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318575**Targeting Sarcomas and Their Progenitors by Mesenchymal Stromal/Stem Cells Based Drug Delivery**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318579**Development of a specific comorbidity index to improve the management of elderly MDS/AML patients**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318595**Promoting neuroplasticity for the symptomatic treatment of patients with Multiple Sclerosis**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318619**The role of PIGF/VEGFR1 pathway in the regulation of inflammatory response and vascular rarefaction in hypertension.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.75

GR-2010-2318624**Early signs and early treatment in Rett syndrome: a functional, imaging and molecular study in young patients and in MeCP2 null Mice.**

Reviewers showed a clear disagreement on the project assessment (21 vs 5.5); however, 21 is much more of an agreeable score. An additional review was performed. Rett Syndrome (RS) is a postnatal progressive disorder with no treatment. RS manifests mainly in girls during early childhood. The majority of RS patients carry loss-of-function mutations in the X-linked gene coding for methyl-CpG binding protein 2 (MeCP2), which regulates epigenetic mechanisms leading to remodeling of chromatin structure thereby controlling gene expression. MeCP2 duplication may also cause severe mental retardation; RS cause this in females and male patients, indicating that both increases and decreases of MeCP2 gene dosage are deleterious for normal brain function. Finally, since MeCP2 loss-of-function mutations have been associated with several other neurological conditions, understanding the pathophysiological alterations underlying RS will be relevant for other neurological disorders. The high relevance of the proposal is self-evident; the scientific quality less so. The hypothesis is framed in broad terminology, too broad to be proved by a single 3 year project. A more focused hypothesis and research project would greatly improve this proposal. The project has 2 aims. Aim 1: To individuate early detection markers for developmental alterations in rodent and human behaviour. Aim 2: To reveal neurobiological substrates of early deficits and analyze the effects of early intervention. The PI mentions hints in literature regarding this objective of this aim. Funded research proposals need more firm ground than hints, either in the literature or through preliminary data. Aim 2 gives no explanation or rationale. An explanation of how MECP2 mice exhibit a syndrome similar to RS is lacking.

The PI has a PhD in Basic and Developmental Neuroscience, obtained in 2009 from the University of Pisa. Since then she's been a post-doctoral fellow at the University of Florence. She lists 4 publications, one of which has no impact factor; her H index is 2. It may be premature for this individual to submit a grant wherein she would be the team leader of the research project as her track record is still limited. This is a premature submission from a junior scientist on an important health problem. Convincing preliminary data are lacking as a good grounding in literature is missing. Rationales are not developed. Milestones do not include the expected in vivo results. Project should be re-submitted with a narrower

and more realistic focus. Given the early stage career of the PI, he/she would benefit of detailing clearer milestones.

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees as final score:15.25

GR-2010-2318660

NIR Laser Therapy in pediatric hemato-oncological patients with oral mucositis induced by chemotherapy: evaluation of clinical efficacy and correlation with modifications of oral microbiota and immunogenic properties of pathogenic microorganisms.

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318715

Potential role of TRPM8/TRPV2 channels in breast and prostate cancers: expression, biophysics and pharmacology

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318718

Protective role of HspB8 in motor neuron diseases (MNDs)

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2318729

Hydrocarbons and kidney damage: potential use of Neutrophil Gelatinase associated Lypocalin and Sister Chromatide Exchange

Reviewers initially expressed discording evaluations. As a result, F2F was performed but reported same critique of the reviewer that assigned lower score, without justification on the new score. So the scientific review committee agrees to perform a new collegially evaluation.

Scientific quality and relevance of the research. The project is of high relevance because it deals with a serious health concern. The overall scientific quality is, however, undermined by flaws in the methodology (see below). Innovative content and originality of the project (in view of the current international literature) Biomarkers research in kidney disease is not a new field, and some of the markers proposed in this study have been already used as indicators of pathology (for a review see for instances Nickolas TL et al., *Curr Opin Nephrol Hypertens.* 2008 Mar;17(2):127-32). The application to a specific cohort of Italian workers is innovative. Methodology and development strategy of the project There are critical concerns regarding the study design. The proposed project involves the recruitment of a very large cohort of cases (5000), in a six-month period. It is highly unlikely that the applicant and his team will meet this goal within the deadline. The cases will not be grouped on the basis of the age; it is not unconceivable that the levels of the stress markers will be higher in older individuals. A further flaw concerns the lack of a clinical follow up that confirming association between the biomarkers and kidney pathology. In addition, the study should address the specificity of these biomarkers, and therefore include patients suffering from other pathologies than those in the kidney that are associated with environmental exposure. This strategy is crucial because several of the proposed biomarkers (e.g. interleukins and DNA damage) are indicators of general downstream phenomena, common to a vast number of disorders. A relatively minor detraction, the project does not involve laboratory personnel to perform the proposed experiments. Numerous publications, even though all in journal with modest impact factor, reflected in a good h- index. Final assessment The proposed study is highly relevant for the funding agency. The study design, however, suffer from crucial weaknesses. In conclusion, the review panel agrees with the score of 11, provided by reviewer 1.

After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:11

GR-2010-2318865

The Lausanne Trilogue Play used as a psychodiagnostic and therapeutic tool in a Neuropsychiatric Unit: an innovative clinical experience working with psichitric children and adolescent

The committee has re-evaluated the project and the score given by the two reviewers during the F2F discussion is collegially confirmed.

GR-2010-2318903**Pharmacological treatments plus mesenchymal stem cell transplantation as novel therapeutic approach in cerebral ischemia**

The less generous reviewer provides cogent and persuasive arguments to support the assigned scores and to carry on the F2F discussion. The review panel fully agrees with the score reached in the F2F process.

GR-2010-2318908**Global proteomic profiling of mood disorders: search for molecular fingerprints to improve diagnosis, prognosis and guide treatment strategies.**

Reviewers initially expressed discording evaluations. An additional evaluation was performed. No comments on inclusion/exclusion for psychotropic drugs. Planned to be carried-out in two different centers (Siena and Pisa). Outcomes of interests are not well-defined. PI has no first-author papers. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:12.0

GR-2010-2318945**Disentangling endogenous resident adult cardiac stem cell biology and aging for clinical protocols of myocardial regeneration without cell transplantation**

The committee agrees with the final score suggested by the two reviewers in the face to face. The project is well written, it is innovative and has a high specific relevance. The major weakness is the lack of preliminary data and there is not statistical justification of the sample size (WP4-5).

GR-2010-2318964**Modeling Leigh Syndrome with induced pluripotent stem cells: novel tools to investigate energetic neuronal metabolism.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319022**Immune gene expression and white matter pathology in first-manic patients before and after treatment. A multimodal imaging genetic study**

Both reviews have merits and although the score is somehow different between the two reviewers. The reviews highlight similar considerations about the proposal being innovative and carried out by an established group of researchers. The committee decides to attribute the average score to this project, which is an appropriate score. After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:8.0

GR-2010-2319031**ErbB2-blockade induces myocardial dysfunction, countered by PDE5-inhibition, and by enhancement of myocytes Ca²⁺ cycling and myofilaments Ca²⁺ sensitivity, and by melusin cardiac overexpression**

Reviewers initially expressed discording evaluations. Additional evaluations were performed. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score 15.5

GR-2010-2319049**Prediction of reading acquisition disorders using behavioral and neurobiological markers**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319077**Role of miRNAs in inflammatory synaptopathy in a mouse model of MS**

After having evaluated the project and considered the reviewers comments, the review panel committee confirmed the score assigned during the F2F

GR-2010-2319084**Smart biomimetic constructs with internal microvasculature for stem cell-based cardiac tissue engineering: a clinical translatable approach.**

Reviewers initially expressed discording evaluations. Additional evaluations was performed. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319097**Strategies To Improve Human Cardiac Stem Cell Regenerative Capacity**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319100**Incidence of Oropharyngeal/oral cancer and Human Papillomavirus (HPV) in Italy and Prevalence of High Risk-HPV in oral exfoliated cells in the general population**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319140**Molecular understanding of E3 ligases involved in signaling and cancer**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319221**Early detection of brain metastases: in vivo advanced MRI markers in breast and lung cancer patients.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319262**New antimicrobial agents targeting antibiotic resistance mechanisms and novel or underexploited targets**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.5

GR-2010-2319274**In vivo confocal microscopy of corneal nerves as a novel diagnostic tool in peripheral neuropathies: correlation with skin biopsy, neurophysiology and clinical findings.**

The applicant is at very early stages in his career, and this is reflected in his track record. This is also reflected by section A.C.2 (publications of the same topic of the project proposal), which lists only 3 relevant article and therefore indicates that the applicant has only very limited experience on the topic. In conclusion, the overall profile is good, yet the score assigned by reviewer code 13003036 (score=1) is over-rated. In this respect, the commission believes that even the stricter evaluation of reviewer code 1710625 (score=2) is very generous, especially in comparison with the evaluations of other proposals in this call. Despite this substantial weakness, this remains a high quality proposal and the Commission agrees with the score reached in the F2F process.

GR-2010-2319327**Bacterial adhesion on orthopaedic prosthetic polyethylenes with different chemical and physical properties**

The evaluation of the grant is good but suffers from some weaknesses in the methodology and in the absence of significant preliminary data that would guarantee the ability of the PIs to address the ambitious project plan presented. The reviewers provided contrasting feedbacks; nevertheless, both referees motivated the assigned score appropriately. On these premises, the scientific panel review accepts as final score 12

GR-2010-2319354**StressAMI - Remote multi-disciplinary management program for outpatients with Coronary Heart Disease (CHD) after acute myocardial infarction (AMI)**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319401**Multisensory modulation of body representations as a proxy to reduce phantom-limb pain in amputees: behavioural, cognitive and neurophysiological studies.**

. The reviewers evaluated differently the project. However, the concerns raised by the second reviewer are well motivated. Additionally, no previous experience suggests a realistic power assessments with regard to the number of subjects required. A statistical plan is missing. The budget seems unreasonable. On these premises, the commission agrees on the final score 14.

GR-2010-2319407**A Janus role of autophagy in Cystic Fibrosis: a new therapeutic approach?**

The committee has re-evaluated the project and its assessments. This research project, presented by a young investigator, aims to investigate the role of autophagy in cystic fibrosis. The committee agrees that the methodology should be improved. In particular the inclusion and exclusion criteria of patients and control groups should be precisely defined. Moreover, the committee feels a concern regarding the real independence of the young investigator since no sufficient details are provided in the personal statement section of the proposal. The scientific review committee agrees on F2F final score

GR-2010-2319457**TARGETING TRIM32 AS A THERAPEUTIC APPROACH IN NEUROMUSCULAR DISEASES**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:11.5

GR-2010-2319661**Novel combinatorial therapeutic approach targeting cancer associated fibroblasts-derived GDF15 protein in prostate cancer models**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319668**Early Detection in Autism Spectrum Conditions**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319770**Surviving ER-stress: lessons from a CMT1B neuropathy model**

After careful consideration of the reviewers comments, the Commission fully agrees with the score reached in the F2F process.

GR-2010-2319831**The neural substrate of transcranial direct current stimulation effects on memory functions in Alzheimer disease. A randomized, controlled study using neuropsychological, [18F]FDG PET and fast optical imaging evaluations.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:19.25

GR-2010-2319851**Psychotherapy and pharmacological interventions in Social Phobia: an fMRI study on neurobiological correlates of treatment-induced remission and of response predictors**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2319865**Characterization of behavioral and neuronal alterations in the prodromal phase of Parkinson's disease to prevent dopamine neurons degeneration**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:12.75

GR-2010-2320019**Biological characterization of onset in Bipolar Disorder: a fMRI study with BDNF polymorphisms and methylation patterns analysis in patients before and after first pharmacological treatment**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2320046**Gastro-intestinal bacteria, obesity and insulin resistance.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2320070**Molecular profiling of malignant tumors of the nose and paranasal sinuses: evaluation of diagnostic, prognostic and therapeutic implications**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:15.75

GR-2010-2320179**Novel tools for evaluation of Type A aortic dissection: from bedside to bench, and back**

The committee collegially reviewed the grant and acknowledged the lack of a careful revision by reviewer 1760223 who failed to identify the quality of the PI and his ability to conduct the study. The PI should have indicated better his recent publications that the study section found through pubmed. The presence of many last authored papers would have been beneficial for the overall evaluation of the grant. The other concern raised by both reviewers is on the feasibility of the study. It is indeed very ambitious in 3 years to go from the in vitro observations on the specimen to an in vivo mouse model to the human patient. The committee endorsed these comments. The study section acknowledges also that the reviewer code 1760223 did not fully justify the reasons for the low scores and decided to raise the average to 10.

GR-2010-2320317**Effect of Glucosamine and Vitamin D on Human Osteoarthritic Cartilage**

Reviewers initially expressed discording evaluations. Additional evaluation was performed. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2320404**Intrauterine growth restriction. Clinical and proteo-metabolomic investigation.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:9.5

GR-2010-2320571**Pathogenesis of West Nile virus infection: a balance between virulence, innate immunity and viral evasion**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:12.5

GR-2010-2320635**Definition of the epigenetic signature in Multiple Myeloma by high-resolution DNA methylation profiling and integrated analysis with genomic imbalance, gene and microRNA expression.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2320639**NEW THERAPEUTIC MODALITIES FOR GRAVES ORBITOPATHY WITH THE ANTI-CD20 MONOCLONAL ANTIBODY RITUXIMAB**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2320668**Role of alternative polyadenylation in cancer**

Reviewers expressed discording evaluations. Additional evaluation was performed. Each of the three submitted reviews points out important issues concerning the application. As highlighted by reviewer code 1718579, the methodology could have been described in greater detail. To level the differences between the reviewers evaluations, the commission recommends a score 12.5

GR-2010-2320674**NeuronHeart Cytoskeletal proteins of neurons confer cardioprotection against myocardial infarction**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2320779**Role of peripheral Schwann cells and muscle in the regeneration of degenerated nerve terminals at the neuromuscular junction.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the final score:7.0

GR-2010-2320783**Obesity-associated Flt3 mutations in Acute Promyelocytic Leukemia: investigating a novel paradigm for the cancer-promoting effect of obesity**

The committee has re-evaluated the project, its assessments and confirms the final score decided by the two reviewers.

GR-2010-2320870 RODDI - New Robotic Platform for Rehabilitation of Children with Pervasive Developmental Disorders and Cognitive Impairments.

The committee has re-evaluated the project and the score given by the two reviewers during the F2F discussion is collegially confirmed. This is an important proposal that could contribute significantly to the field of continuous rehabilitation of children with developmental disorders and cognitive impairments. It is in line with the priorities set forth by the Italian Ministry of Health and the given score is appropriate.

GR-2010-2320890**A novel approach to hand motor, language and interaction rehabilitation in autism spectrum disorders.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:13.75

GR-2010-2320891**Evaluation and modulation of behavioral and neurophysiological markers of alcohol misuse**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2320995**From NAFLD to HCC: mouse model and definition of predisposing and prognostic factors for human liver disease management.**

The committee has re-evaluated the project and its assessments. This research project, presented by a promising young investigator, aims to investigate the progression from fatty liver to hepatocellular carcinoma focusing also on the role of the gut in liver carcinogenesis. The committee agrees that the methodology should be carefully improved. In particular the number of patients, the recruitments plans, the inclusion and exclusion criteria should be precisely defined. Moreover, even the profile of the control groups should be provided. In this view the committee confirms the F2F final score decided by the reviewers.

GR-2010-2321148**Correlation between morphologic alterations of the glomerular filtration barrier and variations of plasmatic and urinary levels of the brain derived neurotrophic factor (BDNF) in rats undergone repetitive transcranial magnetic stimulations (rTMS)**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2321182**Role of the microbiota and peripheral biomarkers in weight restoration and weight maintenance in patients with Anorexia Nervosa.**

The reviewers provided contrasting scores (13 and 4.5), although reviewer code 13003036 (4.5) did not motivated his/her comments or justified his/her assessment. A concern of the scientific review committee is PI current location/employment and where research will be conducted. Budget and goals are not realistic. Specifically, patient recruitment will be covered in year 1, while data collection will start in mid-year 2. There is no realistic time to fulfill the proposed sample analysis and data analysis. F2F is 6.5, however it does not reflect project feasibility. The Scientific Review Committee propose a new final score final 9.0 based upon evaluation.

GR-2010-2321184**TDP43 translocation in response to synaptic activation: a study on wild type and mutant forms.**

Reviewers showed a disagreement on their evaluations of 6 and 11. Final scoring was 9.0, although no F2F discussion was provided. Main critique was that the proposal is not describing the importance and/or innovation of this idea and the relevance of the results that will be obtained by the study. The methodology that will be employed in the study is also not innovative. There is no discussion about possible alternatives if the proposed hypothesis will be disproved. A more exhaustive explanation of which TDP43 mutants will be employed in these studies and their current availability to the PI would have been welcome to better assess chance of success. The scientific review committee evaluated the proposed studies. The PI should narrow down aims to increase feasibility. Aim 2 is too dependent from Aim 1, thus limiting success. In Aim 2, it should be clarified which common ALS-related TDP43 mutations will be studied. In Aim 3 it is not clear which sample and experimental design will be analyzed by immunoblot and co-IP studies. Groups design should be provided to assess validity of the approach and to assess expected findings. After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:11

GR-2010-2321187**IDENTIFICATION OF NEW DISEASE GENES ASSOCIATED WITH BRUGADA SYNDROME BY WHOLE EXOME SEQUENCING**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2321383**Development of algorithms for automatic classification of the ECG signals generated by equipment for telemedicine in order to validate diagnoses in cardiological emergency.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:18.0

GR-2010-2321466**Observational research: Psychological follow-up in living donation process.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2321606**CANNABINOID AND GLUCOCORTICOID INTERACTION: A POSSIBLE BRIDGE OVER TROUBLED DISEASES**

After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:10

GR-2010-2321640**Gold nanoparticles targeting of beta-amyloid plaques in the brain of animal models of Alzheimer's disease**

After having evaluated the project and considered the reviewer comments, the review panel committee agrees on this final score:11

GR-2010-2321666**Transcriptome of B lymphocytes in Multiple Sclerosis.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2321715**The role of Ambra1-mediated autophagy in the development and prognosis of gliomas.**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2321761**In vitro and in vivo physiological cardiac remodelling in response to endurance and strength exercise training**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2321787**Ventricular tachyarrhythmias associated with cardiac hypertrophy and myocardial infarction: implications for early recognition of microRNAs levels and treatment**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2321854**Dissecting microRNA function in mesothelioma development and progression**

Reviewers initially expressed discording evaluations. As a result, F2F was performed and it was appropriate and well documented. The scientific review committee agrees on F2F final score

GR-2010-2321956**INVESTIGATING THE ROLE OF THE CERULOPLASMIN/TRANSFERRIN SYSTEM IN THE PHYSIOPATHOLOGY OF HEPATIC ENCEPHALOPATHY.**

The reviewers expressed discording evaluations of 4.5 and 15. Reviewer code 13003036 (4.5) did not backed up his scoring by providing comments. The Scientific Review Committee re-evaluated the proposed studies and found reviewer code 1710677 appropriate since he/she provided in-depth comments. The scientific review committee agrees on final score 10.0

GR-2010-2322016**Genome-wide association study (GWAS) to identify new disease-causing genes and new susceptibility loci for focal segmental glomerulosclerosis (FSGS) in European population.**

After having evaluated the project and considered the reviewers comments, the review scientific committee agrees on the average as final score:15.25

GR-2010-2322045**Application of multilocus sequence typing (MLST) for surveillance of Candida infections in hospital care units and use of PCR-based methodologies to determine the frequency and distribution of emerging new cryptic Candida species.**

The project aim is relevant from a public health perspective The project involves a highly relevant public health area: surveillance of Candida infections in hospital care units. There is a significant burden attached to such infections in terms of both disability and health care costs The p.i., although relatively young, has good publications in this research area as a first author.

Given the burden of Candida infections and the high cost for the Italian national health system of such hospital infections, a careful characterization of current and emerging Candida infections is a priority for the Italian NHS. A weakness is the absence of a clearly formulated study hypothesis.All in all, more weight has to be given to the evaluation of the first reviewer among the two who have already evaluated the proposal. The committee agrees on a score of 9.5