BrainVectors Newsletter n° 5

Marie Curie Industry-Academia Partnerships and Pathways - Contract n° 286071

BrainVectors dissemination: the Evry EMBO workshop

Modern DNA concepts and tools for safe gene transfer and modification
IBGBI – University of Evry-Val d'Essonne,
Evry, France - 30 March - 3 April 2015

This was the 2nd dissemination event that the *BrainVectors* consortium organized after the **meeting in Madrid** on October 2013, and described in the **NL3.**

This event is framed in the context of a long term training program with initiatives aiming at encouraging PhD students and postdocs to develop their career in gene & cell therapy fields, since 2001.
We stress the importance of this event in Evry, which represents a **milestone** in the history of research-training-innovation triangle in this field. In fact, it was the first time that the gene editing approach was developed in an EMBO workshop and organized by an EC-funded (Marie Curie program) project. Thus, the *BrainVectors* project has amplified the impact of the workshop in showing the progress of industry-academia joint research efforts. Indeed, we achieved a wide sponsorship in mobilizing several national and European academic and private institutions of excellence, foundations, learned societies and SMEs. All together, the above aspects of the event in Evry represent the excellence of our training-dissemination program.

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1. General description of the event

1.1. Summary

Scientific aspects. The workshop reviewed scientific and technical aspects of the new gene therapy approach based on DNA modification at specific sites of genome. The topics were developed by 42 invited speakers, 18 selected short presentation, and 56 posters[1]. In addition to formal presentations, **(a)** two interactive sessions (animated by scientists from Sigma Aldrich) presented the practical aspects of gene editing; **(b)** a panel-discussions (chaired by K. Cichutek[2]) developed ethical and regulatory issues; **(c)** another panel discussion (chaired by A. Trasher[3]) presented the current gene therapy clinical trials. Therefore, this event has been the first one to develop extensively the gene editing approach

Activities. Furthermore, the participants have been involved in networking and social activities: (i) the *Project game*, that was a team-work, where they were divided in groups and elaborated a cooperative project, (ii) visits of the GENETHON and ISTEM facilities in the Evry bio-park and the Evry Cathedral and Museum on 01/04[4], and (iii) cocktails & dinners on 30/03 and 02/04. Globally, most of the time, i.e. ~80 %, was dedicated to oral presentation and poster viewing, and the remaining time to discussions and demonstration of practical approaches (see table 2). Full information on the event (program, abstracts of oral and posters presentations, biographical sketch of invited speakers, exhibitors, sponsors, venue, logistics etc…) is available in section 2 and in the booklet which will be provided to the Commission separately.

Participants. **195 attendees** in total participated in the event (see section 3). 40% of them were young researchers (PhD students and postdocs). Thanks to a massive campaign of information, about half of the participants were from abroad, belonging to academic institutions and industries of 26 countries (see the statistics in section 3). The wide geographical distribution of participants allowed intense interaction between scientists from several institutions and countries and, thereby, this increases the potential of the European Research Area and the chances of employment for young researchers as well.

Logistic. The IBGBI is a new building of the Université d'Evry-Val d'Essonne (UEVE), that made available the conference hall, two rooms were posters and exhibitors were accommodated and some services (technical assistance, parking, cleaning..;). All equipment (cloakroom equipment, computers, audio-video devices…) and other services were made available by the organizers.

1.2. Scientific highlights. The current knowledge on the structure and functions of genome was extensively overviewed to address unresolved questions about gene therapy and, in particular, on the approach of **DNA modification at specific genome sites**. This was achieved by delivering the scientific information in 10 sessions of oral presentations, posters, panel discussions and demonstrations on practical approaches (see section 2). Briefly, during the first 2 days, the speakers delivered general reviews on:

(i) genome organization,

(ii) chromatin structure and dynamics, namely, the recombination events during meiosis and how to interfere with them,

(iii) gene expression and the role of different genetic/epigenetic factors (proteins and RNAs) involved in it.

In the 2nd and 3rd day, the topics focused on how to drive homologous recombination as gene surgery to **correct efficiently and safely** genetic alterations causing inherited diseases and other pathologies. During the sessions 4-6, the proteins involved in gene targeting were extensively reviewed by

[1] Posters were exhibited during all the event duration and viewing/discussions occurred during lunches and coffee times.

[2] He is the most reputed expert worldwide on regulatory issues of gene therapy and biotechnologies.

[3] He coordinates an international platform of clinical trials with patients suffering from hematological disorders.

[4] The participants were split in groups, to allow both visits simultaneously and alternately for each group.

keynote lectures and during Sigma Aldrich's sessions, and ethical and regulatory issues were deeply developed as well. The sessions of the last 2 days focused on **gene transfer**:

(iv) which vectors are suitable for delivering gene surgery tools, such as CRISPER and TALEN proteins and associated factors, into tissues and cells, including stem cells, and

(v) how to use the latter, after appropriate gene modifications, in cell therapies;

(vi) to disclose the interactions between vectors and target cells and tissues: trafficking, gene expression, interferences with cell cycle & differentiation and immune responses against vectors and transgenes, and, thus, define pharmacological settings in terms of benefit/risk for patients.

(vii) To identify and solve specific problems linked to gene transfer into muscle and brain, namely, on the use of inducible promoters enabling the expression of neurotrophic factors in brain, namely, in the ***BrainVectors*** session. Namely, after the introductory talk of Liliane Tenenbaum, 5 invited lectures and 2 communications selected among the young researchers of ***BrainVectors*** consortium, gave an exhaustive picture of the state of the art of gene transfer into brain, according to the work-program of the IAPP consortium.

(viii) To develop experimental conditions and bio-processes to achieve large-scale batches of viral vectors for pre-clinical and clinical studies.

(ix) The ongoing clinical trials and the major issues of the bench-to-clinic road (reliability, efficiency and bio-safety) were presented and discussed extensively in the session 10.

(x) The last session was dedicated to the presentation of the two best posters[5]. These posters described, one, the gene editing approach applied to the dystrophin gene in muscular dystrophies and, the other one, showed the technique of high throughput analysis of RNA editing. In this session, two projects were presented in the context of the *Project game*: one showing possible cosmetic applications of gene editing by changing the eye color, and, the other one, foreseeing site-specific modifications of pain-controlling genes for therapeutic applications. Interestingly, the discussion on scientific, technical and ethical issues arising from the above projects was very intense and highly pedagogic.

1.3. Organization and reaction of the participants.

(i) The sessions started each day at 9h00. At mid-morning, 30-min coffee breaks occurred in the two rooms where the posters and exhibitors were located. The lunches were served also in these rooms from 12h30-13h00 to 14h30. The excellent quality of lunches, coffees, drinks and the service of the catering company (see 5.3.2), allowed the attendees to interact with each other in a pleasant environment. A welcome cocktail-dinner was served on 30/03 to allow the communication between the participants since the first day.

(ii) The accommodations were arranged, for the majority of participants, in the three hotels closest to the IBGBI (Residhome, IbisStyle and ClassEco, at 900 m). Other hotels were available in Evry area and public transportations were available from the hotels to the IBGBI.

(iii) To cut the high density of science, we left free time in the afternoon of the 01/04. During this time we organized visits of the bio-park (GENETHON and ISTEM) and of the Evry Cathedral and annexed *Paul Delouvrier* Museum, guided by members of the Evry City Hall. The conference dinner was organized at the IBIS-Style hotel on April 2nd evening. Pictures showing some moments of the above activities are available in the section 6.

(iv) To reduce the participants' living expenses, we negotiated reduced prices with the hotels in Evry area. Furthermore, we assisted the attendees in booking their hotel, striving to accommodate them in the hotels closest to the IBGBI. In conclusion, although logistic problems noticed by some attendees in their evaluations questionnaire, the event was evaluated **good** or **excellent** by the majority of participants who returned the evaluation questionnaire (see section 5 for extensive description, graphics and comments).

[5] These posters were selected after the evaluation of all participants, who chose 3 preferred posters in a ballot. The organizers identified thus among them the 2 most preferred ones.

1.4. Looking forward. EASCO will promote and support the organization of other events in the next 5 years in Evry, in partnership with local stakeholders of the education, research and innovation, such as the UEVE, Evry Science Innovation, Genethon, Genopole®, Genoscope and the biotech SMEs of the bio-park. We shall strive to attract PhD students and post-docs from abroad, offering them career opportunities with European diplomas, joint thesis and postdoctoral positions, aiming at rendering Evry an international center of excellence on life sciences and biotechnologies. The local authorities (such as the City Hall, Ile-de-France Region and the French Ministry of Education & Research, namely) will be involved not only as sponsors, but also to obtain from them better local infrastructures and services and increase thus the attractiveness of Evry. We fully understand in fact the criticisms of some attendees about the poor quality of logistics and services in Evry, when they said that another place should have been chosen for the EMBO workshop in the event evaluation questionnaires (see section 5.3.2). However, this workshop could not be held in another place than Evry**,** because; first, the tremendous progress that genomic research done in this area since 25 years, produced for life science and, second, for the presence there of excellent institutions, critical mass and resources in this field. Indeed, we expect that the institutions mentioned above will help us in obtaining adequate logistics and services to allow researchers from abroad to stay in an environment worthy of the scientific excellence of its institutions.

Therefore, the organizers will pay great attention to the participants' evaluation feedback, in order to improve the quality of future scientific events organized in Evry and everywhere else.

1.5. Post-workshop dissemination Two tasks are scheduled after this event, in order to amplify the training & scientific impact and foster further development of the program with future initiatives:

(i) to put on line in the www.moderndnaconcepts.org and www.easco.org web sites a report.

(ii) To publish a special issue of *Current Gene Therapy* on early 2016. This issue will contain 9 review-articles contributed by invited speakers, and an introduction article, contributed by the organizers, which will describe the scientific highlights, activities and sponsors.

Both above publications will be sent to the sponsors as soon as these will be available. We shall work on any other dissemination material in the ***BrainVectors*** media such as the newsletters, website and other EC-Marie Curie media eventually.

2. Final program

Day 1 – Monday March, 30th	
8h00 – 9h00:	Registration of participants and set up posters and exhibits. ***Posters and exhibits will be available all the time from March 30th to April 3rd and may be viewed during the coffee breaks and lunches***
9h00– 9h30:	Welcome introduction of organizers and sponsors
Keynote Session 1: ***New DNA visions, technologies and applications*** Chairpersons: S. Fisson and J.F. Deleuze	
9h30 – 10h15:	**Jean François DELEUZE**, Evry (F): *DNA in the new millennium*
10h15 – 11h00:	**Daniel CHOURROUT**, Bergen (NO):*Rapid genome evolution in the sister group of vertebrates*
11h00 – 11h30:	Coffee break / poster viewing
11h30 – 12h00:	**Daniel C. KOBOLDT**, St Louis (MO, USA): *The Next-generation sequencing revolution*
12h00 – 12h30:	**Angela TADDEI**, Paris (F): *Functional organization of the nucleus: lessons from yeast*
12h30 – 14h30:	Lunch / poster viewing
Keynote Session 2: ***Topology and plasticity of genome*** Chairpersons: M. Mezzina and R.. Olhsson	
14h30 – 15h00:	**Hans LEHRACH**, Freiburg (D): *DNA sequencing methods in human genetics and disease research*
15h00 – 15h45:	**Rolf OLHSSON,** Stockholm (S): *The chromatin today*
15h45 – 16h15	Coffee break / poster viewing
16h15 – 16h45:	**Bernard De MASSY**, Montpellier (F): *Genome stability during mammalian meiosis*
16h45 – 17h15:	**Lumir KREJCI**, Brno (CZ): *Homologous recombination from mechanism to pharmacological targets*
17h15 – 17h45:	**Florian PAULER**, Vienna (A) *Genomic imprinting and mammalian epigenetic regulation*
17h45 – 19h15:	**Welcome cocktail-dinner** / Networking

Day 2 – Tuesday March, 31st	
Session 3: ***RNAs and gene expression*** Chairpersons: I. Richard and I. Bozzoni	
9h00 – 9h45:	**Irene BOZZONI**, Rome (I): *Role of non-coding RNAs in muscle differentiation and disease*
9h45 – 10h15:	**Nicole SCHONROCK**, Sidney (AU): *Decoding non-coding RNAs in normal and pathological conditions*
10h15 – 10:45:	Coffee break / poster viewing
10h45 – 11h15:	**Witold FILIPOWICZ**, Basel (Switzerland): *Function and metabolism of microRNAs in mammalian cells*
11h15 – 11h45:	**Pier Lorenzo PURI**, La Jolla (CA, USA): *Epigenetic control of Duchenne Muscular Dystrophy progression by HDAC inhibitors*
11h45 - 12h45:	Selected communications (15' each) **Alfonso JARAMILLO,** Warwick (UK), *Engineering of RNA-based signal transduction in living cells* **Nicolas. WEIN**, Columbus (OH, USA) *Induction of the N-truncated dystrophin by out-of-frame exon 2 skipping prevent or restores muscle function in the Dup2 mouse, providing further support for a therapeutic pathway for 5' DMD mutations* **Vitor CARMONA**, Coimbra (PT) *Ataxin-3 3'UTR reduces neuropathology in a lentiviral mouse model of Machado-Joseph disease - A role for microRNAs?* **Claire DOMENGER,** Nantes (F) *Off-target analysis of a rAAV-U7snRNA vector used for the treatment of Duchenne patients by exon skipping*
12h45 – 1h15:	Lunch / poster viewing
Session 4: ***Gene targeting 1: Biology, technologies and tools*** Chairpersons: K. Charton and C. Mussolino	
14h15 – 15h00:	**Claudio MUSSOLINO,** Freiburg (D) *Targeted Genome Editing*
15h00 – 15h30:	**Emmanuelle CHARPENTIER**, Braunschweig (D) *CRISPR-Cas9 as a new tool for genome engineering*
15h30 – 16h00:	**Jacob G. MIKKELSEN**, Aarhus (DK) *Genome editing by viral delivery of nuclease proteins*
16h00 – 16h30:	Coffee break / poster viewing
16h30 – 17h30:	Selected communications (15' each) **Alejandra GUTIÉRREZ-GUERRERO**, Granada (SP) *Improving gene edition tools for Wiskott - Aldrich syndrome gene therapy.* **David CANO-RODRIGUEZ**, Groeningen (NL) *Locus-targeted epigenetic editing as a tool to reverse epi-mutations in cancer* **Fabien DELACÔTE**, Paris (F) *Optimized tuning of TALEN specificity using non-conventional RVDS.* **Driss. BOUDEFFA,** Monteal (CA) *Doxycycline side-effects on cell size and cell proliferation.*
18h00 – 20h30	**Networking: *Project game***

Day 3 – Wednesday April, 1st	
9h00 – 10h30:	**SIGMA Aldrich workshop I:** *Practical aspects of Targeted Genome Editing: How to be successful!* Presented by **Matthew COUSSENS** St Louis (IL, USA) and **Nadia GUETTARI**, Paris (F)**.**
10h30 – 11h00:	Coffee break / poster viewing
Session 5: ***Gene targeting 2: Applications*** Chairpersons: C. Martinat and B. Péault	
11h00 – 11h45:	**Bruno PEAULT**, Edinburg (UK) and Los Angeles (CA, USA *Multi-lineage Regenerative Cells in Adult Tissues: Prospective Identification, Characterization, Therapeutic Use*
11h45 – 12h15:	**Cécile MARTINAT**, Evry (F) *Use of human pluripotent stem cells for neuromuscular diseases*
12h15 – 12h30:	Selected communication (15') **Juan SONG**, Groeningen (NL) *Targeted silencing of master transcription factor SPDEF to reduce mucus production in airway diseases by artificial transcription factors*
12h30 – 14h30:	Lunch / poster viewing
14h30 – 16h00:	**SIGMA Aldrich workshop II:** *Genome Editing Applications in Drug Discovery and Pre-Clinical Testing* Presentation by **Supriya SHIVAKUMAR,** St Louis (IL, USA) followed by discussions and Q/A exercises with the attendees.

Free time: participants are free to visit Paris or go wherever they want, or **to attend the tours to vsit the Evry city** from 16h00 to 20h00 as follows:

- 16h00 – 18h20: visit to genomic bio-park: Généthon, ISTEM, Genopole
- 18h30 – 20h00: visit to the Evry Cathedral (including organ music)

Day 4 – Thursday April, 2nd	
Session 6: ***Gene targeting 3: Bio-safety of gene editing approach*** Chairman: K. Cichutek	
8h30 – 10h30:	Panel presentations and discussion on: ***Bio-safety, regulatory and ethical aspects of gene targeting: vision for the future*** • **Bruce LEVINE**, Philadelphia (PA, USA): *Preclinical safety evaluation of gene editing for tackling HIV Infection* • **Nicolas FERRY**, Paris (F): *Bio-safety aspects of AAV-mediated gene editing* • **Ute MODLICH**, Langen (D): *Tumorigenicity assays for assessing mutagenic potential of integrating viral vectors* • **Klaus CICHUTEK**, Langen (D): *Gene therapy: guideline for good practice*
10h30 – 11h00:	Coffee break / poster viewing

Session 7: ***Vectorology 1: Current state, perspectives and bio-safety*** Chairpersons : O-W Merten, F. Mingozzi and M. Gonçalves	
11h00 – 11h45:	**Katherine A. HIGH** Philadelphia (PA, USA): *Perspectives on clinical development of viral vectors'*
11h45 – 12h15:	**Federico MINGOZZI**, Paris/Evry (F): *Immune response to vectors and transgenes and tolerance induction*
12h15 – 12h45:	**Christian MEYER**, Amsterdam (NL): *Establishing biosafety profiles of Gene Therapy Products during clinical development and post-marketing: Glybera and beyond*
12h45 – 14h00:	Lunch / poster viewing
Session 8: ***Vectorology 2: vectors development for genome editing*** Chairpersons: F. Mingozzi and D. Stockholm	
14h00 – 14h30:	**Matthew HIRSCH**, Chapel Hill (NC, USA): *The use of AAV vectors for genome editing approaches*
14h30 – 15h00:	**Manuel GONÇALVES**, Leiden (NL): *The use of AdV and LV vectors for genome editing approaches*
15h00 – 16h00:	Selected communications (15' each) **Neelam PANCHAL**, London (UK) *T cell gene therapy for X-linked lymphoproliferative disease (XLP) using a novel transduction protocol* **Saliha MADJOUL,** Evry (F) *Lentiviral gene transfer enhancement using a new family of culture additives: Discovery of Vectofusin® peptides* **Benjamin COGNÉ,** Nantes (F) *rAAV vectors characterization by next generation sequencing* **Ana S. COROADINHA**, Oeiras (PT) *Single step cloning-titration method: enabling tools for virus producer cell line development and engineering*
16h00 – 16h20:	Coffee/tea break / poster viewing
Session 9.1: ***Vectorology 3: Recent advances of vectors applications in diseases*** Chairpersons: C. Le Guiner and M. Hirsch	
16h20 – 16h50:	**Adrian THRASHER**, London (UK) *LV in gene therapy of hematopoietic stem cells diseases*
16h50 – 17h20:	**Caroline LE GUINER**, Nantes (F) ***AAV*** *as potential therapeutics for muscle diseases*
17h20 – 18h05:	Selected communications (15' each) **Céline VANDAMME**, Nantes (F) *Detection and Characterisation of Human anti-AAV CD8+ T Cells using MHC class I Multimer-Associated Magnetic Enrichment* **Annahita KERAVALA,** Menlo Park (CA, USA) *Evaluation of AAV Variants for Intravitreal Administration of Transgenes in Non-Human Primates* **Fedor SVINARTCHOUK**, Evry (F) *Serum proteins and rAAV efficacy.*
20h00 – 23h00:	**Gala dinner at the IBIS Style Hotel /** ***Networking***

Day 5 – Friday April, 3rd	
Session 9.2: ***Vectorology 3 (cont.) BrainVectors: an industry-academia joint project for brain gene therapy*** Chairpersons: A. Das and L. Breger	
8h30 – 8h50:	**Liliane TENENBAUM**, Lausanne (CH) *A next step in neuroprotective gene therapy for Parkinson's disease: adjustment and monitoring*
8h50 – 9h10:	**Ludivine BREGER,** Lund (S) *LVV vectors: from modeling to treating neuro-degenerative diseases*
9h10 – 09h30:	**Felix JUNYENT**, Montpellier (F) *CAV-2 vectors to understand brain function and treat brain diseases*
9h30 – 09h50:	**Cristina PEIXOTO**, Oeiras (PT) *Quality control of viral vectors– overview of characterization methods*
09h50 – 10h20:	Coffee/tea break / poster viewing
10h20 – 10h40:	**Hueseyin FIRAT**, Huningue (F) *Biomarkers for the monitoring of gene therapy clinical trials*
10h40 – 11h00:	**Atze DAS**, Amsterdam (NL) *Tet-On systems for inducible gene expression*
11h00 – 11h30:	Selected communications (15' each) **Marie HUMBERT-CLAUDE,** Lausanne (CH) *Toward a pharmacological control of gene therapy for Parkinson's disease.* **Diego PIGNATARO**, Pamplona (SP) *Road to reconstruct the nigrostriatal pathway in parkinsonian macaques.*
11h30 – 13h30:	Lunch / poster viewing
Session 10: ***Vectorology 4: Viral vectors in clinical trials*** Chairman: A. Thrasher	
13h30 – 16h00:	Panel presentations and discussion on: ***Clinical trials: where we are and what will be the next*** • **Alessandra BIFFI,** Milan (I), *HSC gene therapy for the treatment of metachromatic leukodystrophy and other lysosomal disorders* • **Nathalie CARTIER**, Paris (F), *Gene therapy of leucodustrophy* • **Katherine A. HIGH** Philadelphia (PA, USA): *Genome editing for hemophilia gene therapy* • **Anne GALY,** Evry (F), *Gene Therapy for Wiskott-Aldrich Syndrome: Ongoing International Studies* • **Luca BIASCO**, Milan (I): *Biosafety and biology of engineered cells in gene therapy clinical trials* Conclusion talk: ***Update on current and future clinical trials for gene therapy"***
16h00 – 16h30:	Coffee/tea break / poster viewing
Session 11: ***Networking session : Report on activities*** Chairperson: L Breger	
16h30 – 17h45:	**(i)** 4 PhD students of Evry University present their project: *Gene cosmetology: the ocular gene cosmetology project: a new mean to change the eye color*

	(ii) Presentation of the collaborative projects arisen from the networking activities concerning the "*Project Game*".
	(ii) 2 talks of authors of posters that have won the poster prizes
17h45 – 18h00:	**Mauro MEZZINA Concluding remarks and outlook**
End of the EMBO workshop	

2.1 Presentation and abstracts of *BrainVectors* researchers (Day 5 - Session 9.2: *Vectorology 3 (cont.) BrainVectors: an industry-academia joint project for brain gene therapy*)

Liliane TENENBAUM

Neuroscience Research Center.
Clinical Neurosciences Department, Lausanne University Hospital.
CHUV, Pavillon 3, Avenue de Beaumont, CH-1011 Lausanne, Switzerland
Phone: +41 21 314 1048
Email: Liliane.Tenenbaum@chuv.ch
Web site: http://www.chuv.ch/neurosciences;

Liliane Tenenbaum obtained a PhD (1987) in the Dept of Molecular Biology of the "Free University of Brussels" (ULB). She pursued a post-doctoral training in the Dept of Virology of the Weizmann Institute of Science (Israël) with Prof. Ernest Winocour (DNA replication of "adeno-associated virus"; 1987-89). She continued her post-doctoral training in 2 different laboratories on projects based on parvoviral vector-mediated gene transfer in cancer (ULB, 1990-1992 ; Prof.J.Rommelaere) and demyelinating diseases (Dept Pharmacology, VUB; 1993-1996). She became Responsible of the Laboratory of Neurosurgery (ULB) from 1997 to 2010, developing translational approaches for cellular and gene therapies for Parkinson's and Huntington diseases. From 2003 to 2010, she was also acting as "reference biologist" for the group "Hôpital Erasme" (Prof. Marc Levivier, ULB) in a multicentric clinical trial on transplantation of fetal brain tissue for patients with Huntington disease coordinated by Dr Anne-Catherine Bachoud-Levi.
Since 2010, she moved to Lausanne University Hospital where she is the leader of the group « Gene transfer for Parkinson's disease" in the Laboratory of Cellular and Molecular Neurotherapies (Prof. N.Deglon ; http://www.unil.ch/lcmn/home.html

Research interests Our work aims at developing AAV vectors allowing to take into account pharmacological aspects of brain gene delivery, i.e to fill-in the gap between on-going pioneer clinical trials offering efficient but uncontrolled transgene expression and future safe and adjustable treatments. Focusing on neurotrophic factor delivery in Parkinson's disease, we are i) developing a clinically-acceptable gene switch to control transgene expression and ii) comparing 2 well-established families of viral vectors (AAV and lentiviral vectors) with a new non-human adenoviral vector with distinct advantages.

We are also interested in the role of the brain environment in neuronal cell death, in particular, inflammatory pathways that are overactivated in Parkinson's disease and candidate interfering genes.

Our skills and facilities include: production and titration of laboratory-scale AAV vectors of several serotypes, preclinical rodent models for Parkinson's disease, stereotaxic (intracerebral) delivery of viral vectors and motor symptoms analysis (Center for the study of animal behaviour) as well as post-mortem analyses (immunohistology and cellular imaging facility).

Title of the presentation: *A next step in neuroprotective gene therapy for Parkinson's disease: adjustment and monitoring*

Abstract AAV vectors mediating long-term transgene expression and minimal immune responses in the brain, are excellent tools for gene therapy of chronic neurological diseases. Up to now, clinical trials were based on stereotaxy-guided intraparenchymal delivery of rAAV2 (with the recent exception of the AAVrh10-based gene therapy for San Filippo disease). With the advent of more efficient vectors derived from other serotypes as well as techniques for global brain transduction, novel gene therapy-based treatments are likely to rapidly develop.

Three different paradigms of therapeutic gene delivery for Parkinson's disease have been explored: i) delivering enyzmes of the dopamine biosynthesis in the putamen; ii) synthesizing an inhibitory neurotransmitter (GABA) into the subthalamic nucleus and iii) providing neurotrophic support through neurturin gene delivery in the nigro-striatal pathway. These pioneer clinical trials, together with trials in other brain diseases, have established the safety and tolerability of rAAV delivery in the human brain at moderate doses.

Therapeutic effects however, were modest, emphasizing the need for higher doses of the therapeutic transgene product. However, for more efficient treatments, given the irreversible nature of vector-mediated gene delivery, a pharmacological control of transgene expression will become crucial. Regulatable vectors allowing to adjust the dose and the schedule of the treatment to the patient's needs are currently not clinically available. In addition, targeting transgene expression to specific cell types in the brain is desirable the safety of the treatment, e.g. to avoid transduction immune cells or undesired axonal transport of the vector to off-target regions.

Our goal is to develop clinically-acceptable regulated and targeted viral vectors. The targeting can achieved by combining cell-type-specific and drug-regulated promoters or by disease-inducible promoters driving transgene expression specifically in affected cells.

However, the demonstration of clinical efficacy will be challenging due to the slow and varying progression of Parkinson's disease. An integrated approach combining clinical rating of the patients with molecular biomarkers and brain imaging will likely be necessary to correlate transgene expression with clinical benefits and adjust the dose and time schedule of the treatment in real-time.

Ludivine BREGER

CNS Gene Therapy team
Dept of Experimental Medical Science
Wallenberg Neuroscience Centre, BMC A11
Sölvagatan 17
221 84 Lund, Sweden

Phone: +46 46 222 30 80
Email: Ludivine.Breger@med.lu.se
Web site: www.med.lu.se/expmed/cns_gene_therapy

Post-doctoral fellow of ***BrainVectors***

My academic career has focused on neurodegenerative diseases through translational research, specifically developing therapies for Parkinson's disease. Parkinson's disease is the world's second most common neurodegenerative disorder, characterised mainly by movement impairment, due to localised neuronal death. The current pharmacological treatment, levodopa, only alleviates part of the symptoms and is associated with severe long-term adverse effects, namely abnormal movements (dyskinesias). My main scientific goal is to develop new biotherapies for the treatment of Parkinson's disease.

I was born and initially studied in France where I graduated with a Master's degree specialising in Cell and Gene Biotherapies. When awarded the PhD scholarship by the School of Pharmacy and Pharmaceutical Sciences, I moved to Cardiff University (Wales, UK) to work on cell therapy for Parkinson's disease. This was spared by clinical trials had reporting dyskinesias observed in some patients transplanted with fetal cells. Thus my PhD focused on determining how to reduce the risk of developing side effects, using an animal model of Parkinson's disease, before the upcoming TransEUro clinical trial.

Next I sought to broaden my expertise by working on the potential of gene therapy to slow down neurodegeneration in Parkinson's disease and reduce the development of adverse effects following levodopa treatment. I therefore joined the CNS Gene Therapy Group at Lund University (Sweden) to work on the EU funded project BrainVectors. Part of this project uses lentiviral vectors to express the neurotrophic factor GDNF and improve cell survival in a rat model of the disease. Additionally, one of my most recent projects focuses on using the retrograde transport of lentiviral vectors, presenting rabies envelope proteins, to target specific neurons in an attempt to prevent the development of side effects associated with levodopa treatment.

Title of the presentation: ***LVV vectors: from modeling to treating neuro-degenerative diseases***

Abstract Lentiviruses are able to infect a broad range of cell types and transfer large pieces of genetic material into the host genome. Over the years, they have been manipulated and became a common tool in the field of molecular biology. As they can be engineered to genetically modify cells or organisms, they have been extensively used in attempts to model or counteract disease processes. Because of their ability to transduce non-dividing cell of various pseudotypes, lentiviral vectors provide a potent way to transfer genes in the central nervous system, where most cells have limited proliferation potential. Neurodegenerative disorders, such as Alzheimer's or Parkinson's diseases, affect over 45 million people worldwide. This figure will continue to increase as the world population ages, making research in neurodegeneration a priority in many developed and emerging countries.

Over the past decades, lentiviral vectors have allowed scientists to develop disease's models, using different approaches. Expression of toxic proteins, involved in disease processes, has been used to generate *in vitro* and *in vivo* models of neurodegenerative diseases (e.g. beta-amyloid in Alzheimer's disease or alpha-synuclein in Parkinson's disease). Another approach was to reprogram adult skin cells obtained from patients' biopsies, and use them to generate neurons to study disease mechanisms. Furthermore, if lentiviral vectors constitute a useful experimental tool, they also demonstrate great potential for therapeutic gene transfer in the central nervous system. This talk will explore how the use of viral vectors have revolutionized research in the field of neurodegenerative diseases and discuss the advantages and risks linked to the use of such vectors for the treatment of neurodegenerative diseases.

Felix JUNYENT

Institut de Génétique Moléculaire de Montpellier
CNRS-UMR 5535
1919, Route de Mende
Montpellier, FRANCE
www.igmm.cnrs.fr
Phone: (+33) 04 34 35 96 75
Email: felix.junyent@igmm.cnrs.fr

Post-doctoral fellow of ***BrainVectors***

2004 Degree in Biology at Univesrity of Barcelona on 2004.
2008 PhD in neuroprotective strategies in neurodegenerative diseases done at Cell Biology Department, Faculty of Biology, University of Barcelona.
2008-2013 Postdoctoral researcher to study the molecular mechanisms involved in neuronal death in neurodegenerative diseases at Centro de Investigaciones Biomedicas en Red en Enfermedades Neurodegenerativas (CIBERNED), Barcelona.
2009-2013 Associate lecturer at Department of Biochemistry of University Rovira i Virgili, Tarragona.
2013-2015 Postdoctoral researcher involved in the generation of CAV-2 vectors to study brain functions and to treat brain diseases, at IGMM, Montpellier.

Title of the presentation: ***CAV-2 vectors to understand brain function and treat brain diseases***

Abstract Canine adenovirus type 2 (CAV-2) vectors are powerful gene delivery tools for fundamental and applied neurobiology due to their preferential transduction of neurons, widespread distribution via axonal transport, >1 year and 6 month duration of expression in the

brain of rodents and nonhuman primates, and minimal immunogenicity. CAV-2 is internalized in neurons by the selective use of coxsackievirus and adenovirus receptor (CAR), which is expressed by neurons in the brain parenchyma. CAV-2 axonal transport is likely mediated by CAR at the synapse potentiating vector biodistribution. The above characteristics, together with the 30 kb cloning capacity makes helper-dependent (HD) CAV-2 vectors powerful tools to treat neurodegenerative diseases. We will present examples of HD CAV-2 vector efficacy, in particular a) a vector expressing □-glucuronidase (GUSB) which was used to correct the neurological defects associated with mucopolysaccharidosis (MPS) VII in the murine and canine MPS VII brain; b) vectors harbouring doxycycline-inducible GFNF expression cassettes to promote the dopaminergic neuron survival in Parkinson's disease and c) their use to understand higher order cognition and behaviour.

Cristina PEIXOTO

IBET, Oeiras, Portugal

Phone: + 351 21 446 94 57
peixoto@ibet.pt
http://www.itqb.unl.pt/labs/animal-cell-technology/

Cristina Peixoto graduated in Applied Chemistry (Branch Biotechnology) New University of Lisbon and holds a PhD in Engineering Sciences from Instituto de Tecnologia Quimica Biológica (ITQB).
Main Scientific activities: Development and optimization of purification and characterization of different products with applications as therapeutics or vaccines associated with several biological systems. Approx. 40 publications in refereed journals.
Since 2009, Cristina Peixoto is responsible of the downstream process development and characterization of complex biopharmaceuticals at Animal Cell Technology Unit at IBET (Instituto de Biologia Experimental e Tecnológica), Project Manager in research contract projects with Industrial partners and Team member of several Portuguese FCT-funded research projects and EU project consortiums.

Title of the presentation: *Quality control of viral vectors– overview of characterization methods*

Abstract One of the main challenges for translation of promising research in gene therapy to clinical development is the establishment of appropriate quality control (QC) test methods to characterize clinical grade vectors. Controls and validated procedures that relate to clinical viral vector safety must be established early in process development. As clinical development progresses, the knowledge gained from manufacturing experience and product and process characterization studies should be reflected in final cGMP controls. This incremental strategy is based on recognition that some of the information and data required to validate manufacturing processes and analytical methods are obtained during the process (up and downstream) development period. Also, more complex techniques like Atomic force microscopy (AFM), Raman or NMR, traditional applied to other molecules can contribute to increase the knowledge and characterization of final product and product-related impurities. This presentation focuses on QC testing, providing an overview of characterization methods for early phase clinical studies and descriptions for selected assays that are useful to assess vector safety, potency, and purity.

Hueseyin FIRAT
FIRALIS SAS,
35 rue du Fort
68330 HUNINGUE
FRANCE

Phone: +33 (0)3 89 911 321
Email: hueseyin.firat@firalis.com
Web site: http://www.firalis.com

Hüseyin FIRAT is a pediatrician and practiced as an associate professor in Paris University hospitals. After his PhD of Immunology at Pasteur Institute, he was accredited as research director, responsible of the Immunology Laboratory at Généthon. In 2002, he joined then the Biomarker Department of Novartis Pharma, where he headed global omics data analysis sections worldwide, served as senior Biomarker Expert in International Project Teams and was member of Novartis Pharma Innovation Team, Basel. His research activities generated several patented discoveries, based on which three biotech companies have been created. He is the CEO and CSO of Firalis SAS, a biomarker R&D company that he founded with his ex-colleagues in 2008, and manages since then, in coordination with several business and scientific advisors. He also manages as Administrator, TcLand Expression SA.

Title of the presentation: ***Biomarkers for the monitoring of gene therapy clinical trials***

Abstract Over the past decades, gene therapy approaches have been considered for the treatment of a variety of diseases. However, there are significant challenges to transfer preclinical results into clinically acceptable treatment. Among these challenges, immune response against transgene and vector constituents is a key parameter that needs to be addressed for an efficient gene therapy allowing a long term *in vivo* transgene expression.

BrainVectors aims devising new gene therapy (GT)-based treatments for Parkinson's disease (PD), by delivering GDNF (glial cell-derived neurotrophic factor) into the Central Nervous System (CNS) with vectors derived from adeno-associated (AAV), canine adenoviruses (CAV-2) and lentiviruses (LV) with inducible gene expression. Indeed, compelling evidence have been accumulated in numerous studies suggesting that GDNF may ameliorate PD symptoms if expressed correctly.
Within the *BrainVectors* consortium project, Firalis aims to compare immune safety of three gene therapy vectors encoding for GDNF. Such a comparative study on gene transfer into the CNS to establish the pharmacological properties (efficiency and bio-safety) of three viral vectors (AAV, CAV-2 and LV) has never been performed in a preclinical setting.

Based on a multistep approach, we investigated the immune response against a transactivator cassette. To do so, we predicted *in silico* the class I major histocompatibility complex (MHC) HLA-A*0201 restricted epitopes within rtTA TransActivator. Then HLA-A*0201 binding assays are performed *in vitro* on T2 cells. Finally, *in vivo* analysis was carried out in HLA-A*0201 humanized mice to select a set of immunogenic peptides. A similar approach will be used to screen for immunogenic peptides in the different constructs generated within the *BrainVectors* consortium.
We developed tools to follow immune responses against the transgene GDNF during the clinical study such as measure of epitope specific T cell count using HLA-A2.1 restricted peptide loaded tetramers and functional T cell counting using epitopic peptide-loaded APCs and ELISPOT essays.

Ultimately, these findings will generate Biomarker based tools to track immune responses against the transactivator, to allow personalized therapeutic approaches using various immune-modulators and to improve safety monitoring of the gene therapy clinical protocols.

Atze DAS

Laboratory of Experimental Virology, Academic
Medical Center, University of Amsterdam, Meibergdreef 15,
1105 AZ Amsterdam, The Netherlands

Phone: +31 20 5663396
Email: a.t.das@amc.uva.nl
Web site: www.amc.nl

HIV replication and vaccine development. This research line includes both basic and applied HIV research, which are not separated but intermingled and complement each other perfectly.

Basic research focuses on the structure and function of the HIV genome. In particular, we investigate the structure of the viral RNA and its role in different replication steps, such as gene expression, RNA dimerization and packaging. Furthermore, we study the role of the viral Tat protein in replication.

Applied research focuses on the development of an HIV vaccine, novel strategies to inhibit HIV replication and new gene regulation systems. We develop conditionally replicating HIV variants as a novel approach toward a safe live-attenuated HIV vaccine and as a tool to study the immune and other host responses that correlate with protection induced by live-attenuated virus vaccines. We study the application of RNA inference as a novel antiviral strategy. Furthermore, we use viral evolution as a tool to develop new gene expression systems. Such technology for the regulation of gene expression is important for biological/biomedical research, gene therapy and biotechnology applications.

Title of the presentation: *Tet-On systems for inducible gene expression*

Abstract The doxycycline (dox)-inducible Tet-On gene expression system is widely used in both basic and applied biological research in mammalian cells. The Tet-On system is based on the regulatory elements that control the activity of the Tet operon in bacteria. Since its initial construction, this system has been significantly improved for its function in eukaryotic cells. We previously constructed a dox-controlled HIV-1 variant by stably integrating the components of the Tet-On system (i.e. the dox-dependent transcriptional activator rtTA and the tet operator binding sites) in the viral genome and inactivation of the natural transcription mechanism of the virus. Evolution of this HIV-rtTA virus upon long-term culturing resulted in several optimized rtTA variants [1, 2]. To identify the optimal Tet-On system for diverse applications in mammalian cells, we compared old and new Tet-On variants in several frequently used cell types that were either transiently transfected with the relevant plasmids or stably transduced with an "all-in-one" lentiviral vector. We demonstrate that the V10 variant is optimal when the DNA is episomally present upon transfection, because rtTA-V10 demonstrated no background activity without dox, high dox-induced activity, and highest fold-induction. However, the V16 system may be preferred if only low intracellular dox concentrations can be reached, because of the very high dox-sensitivity of rtTA-V16. When the Tet-On components are stably integrated in the cellular genome by lentiviral transduction, the V16 variant performs optimally, because this rtTA lacked background activity and demonstrated highest activity and dox-sensitivity. Moreover, V16 demonstrated more robust induction of gene expression after a period without dox.

[1] Das AT, Zhou X, Vink M, Klaver B, Verhoef K, Marzio G, Berkhout B: Viral evolution as a tool to improve the tetracycline-regulated gene expression system. J Biol Chem 2004, 279(18):18776-18782.
[2] Zhou X, Vink M, Klaver B, Berkhout B, Das AT: Optimization of the Tet-On system for regulated gene expression through viral evolution. Gene Ther 2006, 13(19):1382-1390.

Marie HUMBERT-CLAUDE
PhD, Pharmacist

Neuroscience Research Center.
Clinical Neurosciences Department, Lausanne University Hospital.
CHUV, Pavillon 3, Avenue de Beaumont, CH-1011 Lausanne, Switzerland
Phone: +41 21 314 1048
Email: marie.hubert @chuv.ch

Post-doctoral fellow of ***BrainVectors***

Title of the presentation: ***Toward a pharmacological control of gene therapy for Parkinson's disease.***

Abstract The safety and tolerability of AAV vectors as tools for gene therapy in the brain has been established by several pioneer clinical trials. However, for some therapeutic genes, prolonged uncontrolled expression can lead to adverse effects. Therefore, given the irreversibility of the administration method, gene expression should be adjusted to the patients needs and if necessary, arrested.
A clinically-acceptable genetic system allowing to control the concentration of the therapeutic gene product does not exist. The main challenge is to obtain a genetic switch responding to a clinically-approved drug inducer at a dose which does not elicit adverse effects.
The BrainVectors group has developed a highly sensitive inducible AAV vector whose activity depends on the antibiotic doxycycline (AAV-DoxON).
We are evaluating the potential of this new vector for pharmacologically-controlled gene therapies in a neuroprotective therapeutical approach consisting in the delivery of a transgene coding for a neurotrophic factor called "GDNF" in the striatum, a target brain region for the treatment Parkinson's disease.
Combining a single AAV-DoxON-GDNF intracerebral injection by stereotaxic neurosurgery and oral treatment with doxcycline resulted in a drug dose-dependent GDNF concentrations in the striatum. Strikingly, our data suggest that biological effects of GDNF relevant to its therapeutic efficacy can be obtained with clinically-approved sub-antimicrobial doses of doxycycline commonly prescribed for long-term treatment of inflammatory diseases of the skin (Rosacea) and of the teeth surrounding tissue (Periodontitis).

Diego PIGNATARO LOPEZ

Center for Applied Medical Research (CIMA and Ciberned). University of Navarra
Avenida Pio XII, 55. 31008. Pamplona, Spain.
jpignataro@alumni.unav.es

Title of the presentation: ***Road to reconstruct the nigrostriatal pathway in parkinsonian macaques***

Introduction: The field of Gene Therapy in the CNS has recently witnessed a number of major conceptual changes. At present, ongoing strategies are focused on using vectors carrying genes to further modify brain circuits of interest. It is expected that these approaches will result in a great therapeutic potential being sustained by the induced changes in brain circuitry. Indeed, for the first

time these advances will allow the implementation of "disease-modifying" therapies, e.g., trying to arrest or even revert the natural course of Parkinson's disease.

Experimental approach: Here we are using hRheb(S16H)-carrying Adeno-associated virus (AAV) vectors in parkinsonian macaques, in an attempt to reconstruct the damaged nigrostriatal pathway.

Results: Preliminary results reported here stand on the intracerebral delivery of h-Rheb-carrying AAV serotype 5 in the substantia nigra of two MPTP-treated macaques showing a severe parkinsonian syndrome. After a follow-up of six months, both macaques showed a lack of motor improvement, together with no changes on the conducted microPET neuroimage scans. However, the histopathological analysis revealed a moderate degree of axonal reinnervation in the putamen nucleus following a viral infection limited to 10-12 dopaminergic neurons per animal.

Discussion: These results, so far insufficient to elicit any motor/neuroimage improvements, are very appealing and indeed represent the first evidence that a damaged dopaminergic circuit can be reconstructed in adult parkinsonian macaques. A number of ongoing strategies are currently under development in an attempt to improve the amount of neurons being infected with the hRheb gene, therefore leading to a more complete reconstruction of the nigrostriatal pathway.

Bibliographic references:

1. Burke RE, O'Malley K. (2013). Axon degeneration in Parkinson's disease. Exp. Neurol. 246: 72-83.
2. Kim SR, ET al. (2012). AAV transduction of dopamine neurons with constitutively active Rheb protects from neurodegeneration and mediates axon regrowth. Mol. Therapy, 20: 275-286.
3. Kim SR, et al. (2011). Dopaminergic pathway reconstruction by Akt/Rheb-induced axon regeneration. Ann. Neurol., 70:110-120.

3 Participants

3.1 Statistics and geographical distribution

Nationalities of participants & invited speakers (or country of work)	**PARTICIPANTS**		**INVITED SPEAKERS**		
	# male	**# female**	**# male**	**# female**	**subtotal**
From academia:					
Australia	0	0	0	1	1
Austria	0	0	1	0	1
Belgium	0	1	0	0	1
Canada	1				1
Czech Republic	0	0	1	0	1
Denmark	0	0	1	0	1
Finland	1	0	0	0	1
France	26	51	5	5	87
Germany	1	4	4	2	11
Greece	0	0	0	1	1
Italy	4	3	1	2	10
Latvia	0	1	0	0	1
Netherlands	4	3	2	0	9
Norway	0	0	1	0	1
Poland	1	0	0	0	1
Portugal	1	2	0	0	3
Slovenia	0	1	0	0	1
Spain	2	2	0	0	4
Sweden	1	1	1	1	4
Switzerland	1	1	1	1	4
Turkey	1	1	0	0	2

United Kingdom	7	5	1	0	13
USA	1	0	5	1	7
			subtotal of participants from academia		**166**
From industry :					
France	5	4	1	1	11
Hungary		1			1
Ireland		1			1
Italy		1			1
Lituania	1	0			1
Netherlands		1	1		2
Portugal		2		1	3
Russian Federation	1				1
Sweden	1				1
United Kingdom	1	2			3
USA	1	1	1	1	4
			subtotal of participants from industry		**29**
TOTAl (# male and female)	63	89	26	16	
TOTAl (# participants and # invited speakers)	**151**		**42**		**195**

Table 3: Distribution of participants by country and graphical representation

Pays	%	Pays	%	Pays	%	Pays	%
Australia	0.51	Austria	0.51	Belgium	0.51	Canada	0.51
Czech Republic	0.51	Denmark	0.51	Finland	0.51	France	50.51
Germany	5.61	Greece	0.51	Hungary	0.51	Ireland	0.51
Italy	5.61	Latvia	0.51	Lithuania	0.51	Norway	0.51
Poland	0.51	Portugal	3.06	Russian Federation	0.51	Slovenia	0.51
Spain	2.04	Sweden	2.55	Switzerland	2.04	The Netherlands	5.61
Turkey	1.02	United Kingdom	8.16	USA	5.61		

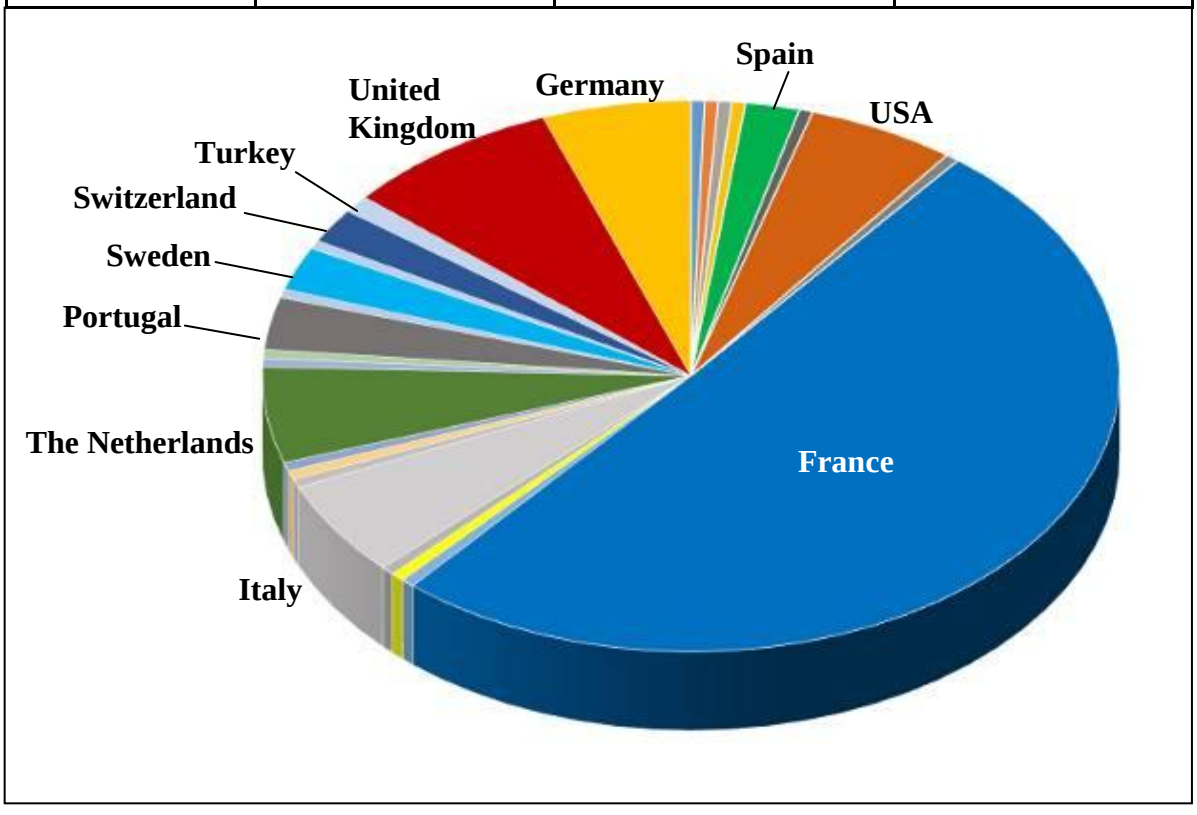


Table 4: Institutions of the participants from the industry

Industrie	Ville(s), pays	pts	Industrie	Ville(s), pays	pts
AVALANCHE	Menlo Park, USA, CA,	2	**OXFORDBIOMEDICA**	Oxford, UK	3
BIOCAD	Saint Petersburg, RU	1	**SANOFI**	Paris, F	6
CELLECTIS	Paris, F	1		Vitry sur Seine	1
CRUCELL	Leiden, NL	1	**SIGMA ALDRICH**	St Luis, USA, MO	2
FIRALIS,	Huningue, F	2		Stockholm, S	1
IBET	Oeiras, PT	3		Galloway, IR	1
LIFE SCI. Techn.	Vilnius, LT	1		Saint Quentin, F	1
MOLMED	Milan, I,	1	**UNIQURE MV**	Amsterdam, NL	1
NEBIOLAB	Budapest, HU	1			

4. Participants' evaluation of the event

91 questionnaires (see the model in 4.1 below) have been returned to the organizers with the responses to the questions and comments. The results of this evaluation are presented by: **(i)** drawing all responses with graphics shown in 4.2 and **(ii)** summarizing the comments relative to the questions in 5.3.

To draw the graphics, points from 0 to 4 were given to the responses, according if these were "*unsatisfactory*" to "*excellent*", respectively, to the questions 1- 5 and 8 – 10, and 1 point was given for each "*Yes*" to questions 6.1, 6.4 - 6.7, "*No*" to 6.2 and 6.3, and for "*right*" to question 7, as indicted below. Therefore, the maximal possible score in a questionnaire could have been **40/40** and the maximal score for each question was **4/4** for questions 1-5 and 8-10 and **8/8** for questions 6 and 7 together.

4.1 Model of the evaluation questionnaire

EMBO workshop: ***Modern DNA concepts and tools for gene transfer and modification,***
IBGBI, Evry University, France, 30 March – 03 April 2015

Name of participant (optional):…… City/country:……
You participated as**:** **attendant** ○ **invited speaker**○ **sponsor**○

---

1. Quality of the program:
unsatisfactory ☐ poor ☐ adequate ☐ good ☐ excellent ☐

Comments on the overall program and/or single session:……

2. Quality of formal presentations (subjects adequately covered, quality of slides etc…)**:**
unsatisfactory ☐ poor ☐ adequate ☐ good ☐ excellent ☐
Comments (name good or bad presentations): ……

3. Was there adequate discussion after each presentation, at the end of each session?
unsatisfactory ☐ poor ☐ adequate ☐ good ☐ excellent ☐
Comments: ……

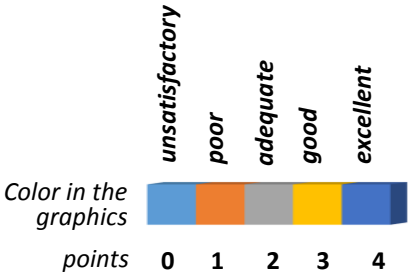
4. Did the workshop fulfill your expectations?
unsatisfactory ☐ poor ☐ adequate ☐ good ☐ excellent ☐
Comments: ……

5. Quality of the IBGBI: conference hall, slide projection, other visual aids, acoustic, posters/exhibit spaces, services etc…
unsatisfactory ☐ poor ☐ adequate ☐ good ☐ excellent ☐
Comments: ……

6. Was there	**Yes**	**No**
6.1 sufficient information available about the workshop?	☑	☐
6.2 any problem with transportation?	☐	☑
6.3 any problem with the workshop language?	☐	☑
6.4 enough time for informal discussions with other participants?	☑	☐
	☑	

Legend to the graphics in 4.2

Questions 1-5 and 8-10



Questions 6 and 7

6.5 enough time for discussion during poster sessions? ☐
6.6 opportunity for discussion with lecturers? ☑ ☐
6.7 opportunity to implement your work and career(new collaborations &projects, new mobility tenures, new jobs…)? ☑ ☐

1 point

Please, provide comments about the one or more points above: ……

7. Duration of the workshop:
right ☑ too long ☐ too short ☐ should be ☐: ……
Comments: ……

8. Accommodation and location (hotel, public services and facilities in Evry….:
unsatisfactory ☐ poor ☐ adequate ☐ good ☐ excellent ☐
Comments: ……

9. Quality of networking and internal communication (*Project game*, visits, social):
unsatisfactory ☐ poor ☐ adequate ☐ good ☐ excellent ☐
Comments: ……

10. Give your overall evaluation of the workshop:
unsatisfactory ☐ poor ☐ adequate ☐ good ☐ excellent ☐
Any additional comments: ……

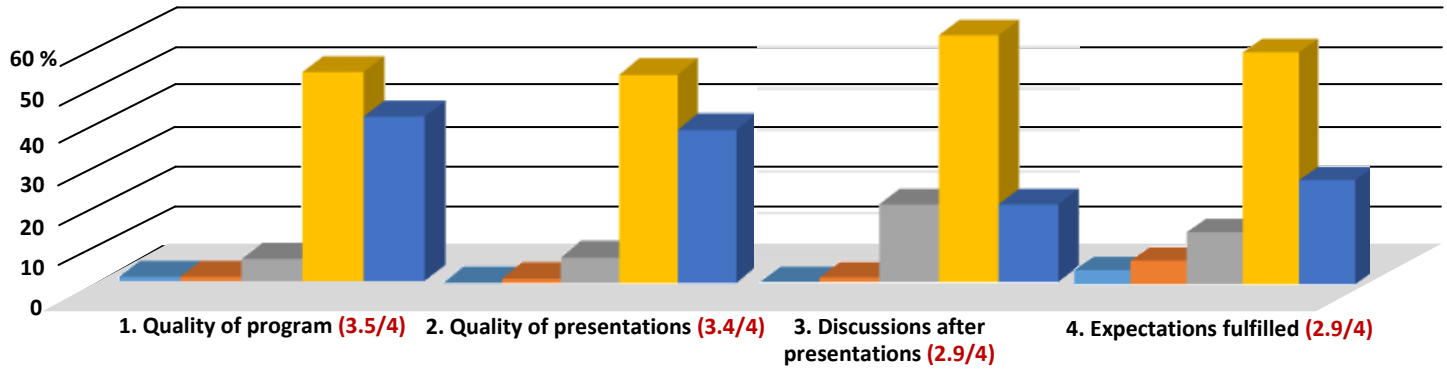
11. If this workshop were to be repeated, what changes would you suggest?
(Comments only)……

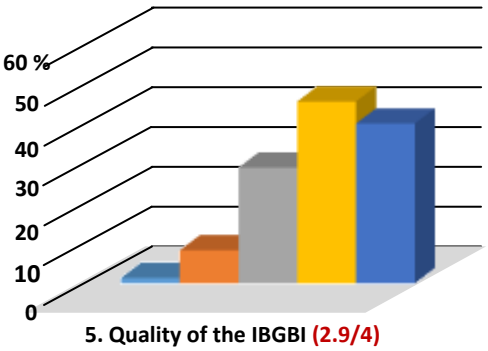
12. We would appreciate any additional comments or suggestions:
Comments only)……

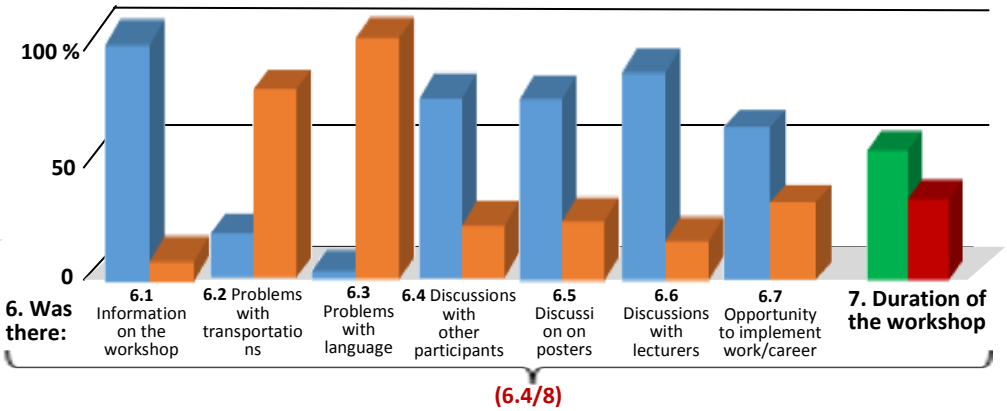
Please, put the filled questionnaire in the box in the reception desk. You will receive the questionnaire also by email and you may send it also to mezzina@easco.org

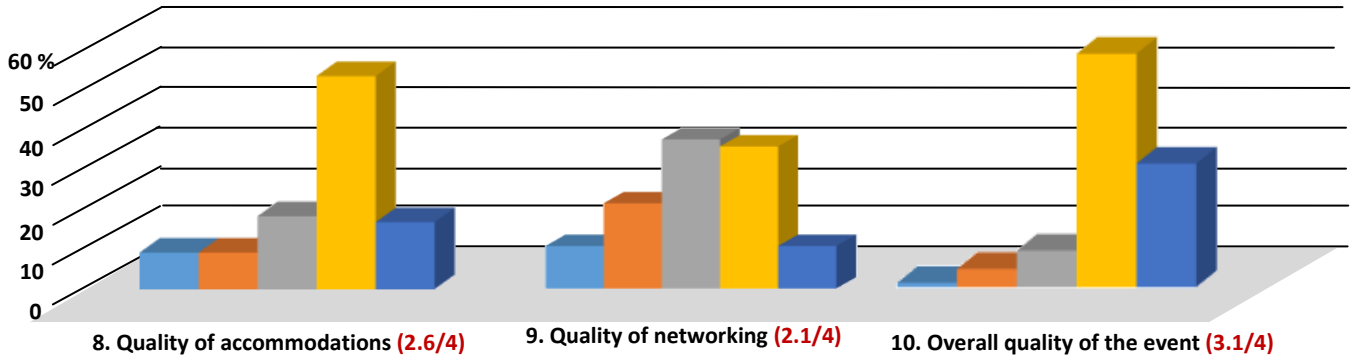
Note that you will be asked also by EMBO to fill up their questionnaire
Thank you for your cooperation

4.2 Graphical representation of results Values in the y axis are the % of the total responses. Numbers in parenthesis indicate the average score obtained.









4.2.1 Conclusions:

1. The average score obtained in the 91 questionnaires was of **29.8/40**

2. The strengths were the quality of the **program** and of **presentations**, with scores of **3.5/4** and **3.4/4**, respectively. The average score of **overall workshop** was of **3.1/4**. The distribution of responses to these 3 questions was quite homogeneous with high frequency of *"good"* and *"excellent"*.

3. The weaknesses were the quality of **accommodations** and of **networking**, which obtained scores of **2.56** and **2.1/4**, respectively, with a heterogeneous distribution of choices, however.

4.3 Synthesis of the comments Among all questionnaires, 16 were without comments and 31 contained 1 or 2 comments only. The 44 other questionnaires contained an average of ~5 comments/questionnaire, for a total of 257 comments. In the paragraphs below, the comments were grouped by question or theme and we added some remarks (text in *italic blue*) to complete the information.

4.3.1 Scientific comments:

● Quality of program: > 90 % of the comments concerning the question n° 1 cheered the quality of the scientific program. The attendees enjoyed the excellent overviews on the state-of-art of the different topics and the top-level speakers. A couple of them have been disappointed by the last-minute cancelation or replacement of some speakers, and two others wrote that hearing more about translation to pharmaceutical applications would have been perfect. *These remarks show the increasing interest of young researchers in translational research. We are aware of the importance of it, but we couldn't allow developing more the industrial applications, due to time limit.*

● Quality of presentations: This also was unanimously appreciated. However, some comments noticed that the density of topics leaded to some delay in the timing during the first day; they noticed some technical problems with microphones and slides projector, solved rapidly, however. *These questionnaires indicate that all attendees were fully satisfied of the scientific program and of the quality of the speakers, which was our priority in fact: an exhaustive overview on the genome, to understand better technologies and applications, rather than focusing on industrial applications.*

● Discussions after presentations: Some attendees noticed that sometimes the presentations were longer than the scheduled time, shortening thus the time for discussions (especially in the first day when some technical video/audio small accidents occurred). An attendee suggested that it should be good to conclude each session with a round table discussion with all speakers to present translation perspectives of industrial/medical applications. *The suggestion of this attendee is very interesting, since such round tables fit well in the format of the workshop. We shall take into account of it in future workshops.*

4.3.2. Logistic issues:

● The quality of catering (food, coffees, drinks) and service provided by the *GUYOT Traiteur* was **unanimously acclaimed**. Everybody appreciated the diversity and quality of food served every day, as well as the politeness and efficiency of the waiters. Furthermore, special menus served to participants having food restrictions, were highly appreciated. .

● Quality of the IBGBI Some comments were about the insufficient space in the rooms were posters were exhibited and lunches & coffees were served as well. Some participants would have appreciated much more the availability in the IBGBI of a room for lunch and coffees, another room for posters viewing and another one to work on the *Project Game*. Some attendees noticed the absence of places where people may

seat around a table and discuss during lunches & breaks. However, services (parking, cloakroom, computers, internet, cleaning) and technical assistance were acknowledged as excellent, *We fully agree with these comments and we expected them, although they were among the less frequent (see table 6, question 5),. The colleagues of the UEVE will transmit such comments to the President of the University to allow more space (rooms, namely), when future meetings will take place in the IBGBI.*

- Quality of accommodations Many attendees were not happy that the workshop was held in Evry, because this city is not very friendly, without places where dining or socializing in the evening. The comments concerned often the distance between the hotel and the IBGBI, obliging to take public transportations or walk for 25-30 minutes. Four other comments concerned the poor quality of their hotel. *As anticipated above, this is one of the **weakness** of the workshop. Although several good hotels are located in Evry area, they are dispersed far from the city center and their quality, i.e., not always worthy of a 3-star category establishment. This engenders dissatisfaction of the customers, as some our attendees have noticed in their questionnaire, rating "unsatisfactory" or "poor" the quality of hotels. Although several attendees found the accommodation good or excellent, however, we are fully aware of this issue and shall face it in our next events.*

- Quality of networking In some comments the attendees said again that they would have preferred that poster viewing would have occurred in specific sessions by theme separated from the lunch and coffee times. Other comments concern the *Project Game*: several attendees stressed their interest for this new concept (*it is a great idea!...*), but the lack of time and of a specific place in the IBGBI to work on it reduced their active participation compared to what they would have liked to do. Several other comments noticed here the poor socializing opportunities in Evry. *In several previous events we organized poster viewing in the same place of lunches and coffee breaks and we got positive feedback each time. We shall take care to organize these activities more comfortably in future, taking into the account of all these suggestions here. Please, note also that the attendees giving such comments here combined probably the scarce spaces in the IBGBI with the poor socializing opportunities in Evry, which may have affected in some of them the overall perception of poor communication within the workshop.*

4.3.3 Conclusion comments

- Expectation fulfilled All comments on this issue stressed that the expectations were totally fulfilled concerning the scientific aspects of the workshop. Most of them suggested, however, that choosing another location with more socializing opportunities, dedicating more space and time to the poster sessions and networking (the *Project Game*, namely) would have enhanced the satisfaction of these participants. *Again, we are fully aware that, even if scientific expectations were fully satisfied, some organizational improvements will be necessary*.

- Overall quality of the workshop: This workshop has a very good overall evaluation, supported by the excellence of the scientific program and of the internationally top-level speakers. Nevertheless, progress should be done in the future to improve the logistics. Suggestions were made in fact about organizing the visits and gala dinner at the beginning of the workshop to allow people to socialize more and enhance thus interactions and networking between attendees. *Our general conclusion after these comments is that the organization of a scientific event engages the responsibility of not only the organizers, who are scientists, but also of all other stakeholders, such as promoter institutions, companies providing infrastructures & services and local authorities responsible for the public security, transportations and recreation, to provide the best conditions to welcome the participants. It is sufficient that an accident happens in a hotel or in the metro, as the participant victim of the accident, gives a negative evaluation of the whole event and he/she keeps a negative memory. Only with the joint work of all stakeholders, we can foresee problems in advance, avoid accidents and achieve excellence in future events.*

5. Picture of the events

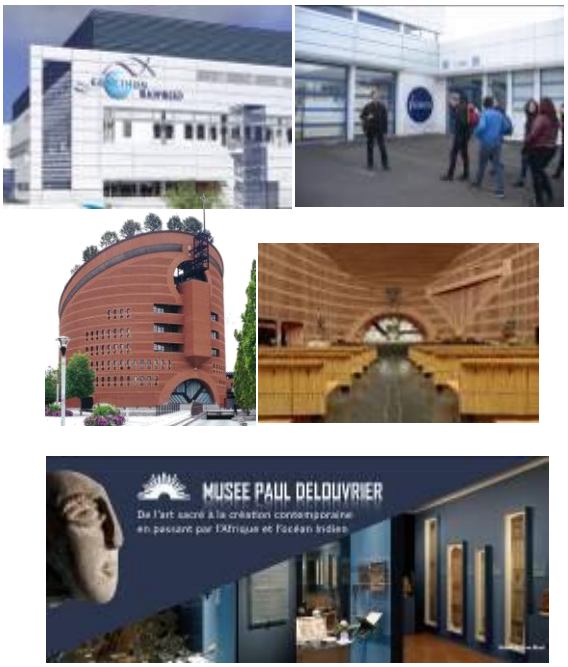
This section contains, in addition to the pictures showing the activities during the workshop. In the pictures in the right side of this page the reader can see images of the IBGBI were these activities were carried out, i.e. the image of the building viewed by outside, the conference hall and the space in the inlet.

30 additional images have been shared in groups according to the activities during the scientific sessions and to other activities.

(i) In the 1st group, ***Conferences*** (images n° 1 – 5), the pictures show the audience in the conference hall (n° 1, 2) and the speakers delivering their lecture (n° 3 - 5). Please, note that photos have been taken during the overall duration of the meeting to all speakers, namely, during their lecturers. These photos are available for any eventual publication, eventually.

(ii) Pictures n° 6 – 9, the 2nd group, ***Poster viewing***, have been taken in the two rooms where the posters and exhibit spaces were located, as described in the previous sections.

(iii) the pictures n° 10 – 23 show the **networking and social activities** of the attendees. In the afternoon of the 1st April the attendees were shared in groups and guided to visit the facilities of **GÉNÉTHON** (pictures n° 10 – 12) and **ISTEM** (n° 13 – 16). Please note that the picture in the right side here displays the arrival of the first persons at the ISTEM. Since the vicinity of these two institutions (located and 100 m from each other in the bio-park), each group visited the two laboratories, another in turn, from 16h30 to 18h15. The visit of the **Evry Cathedral** and the annexed ***Paul Delouvrier*** **museum** (bottom photo in the last right side group here) occurred from 18h30 to 20h00 and is presented in the pictures n° 17 – 20. Finally, the pictures n° 21 – 23 show some moments of the cocktail and dinner on April 2nd evening, at the Ibis-Style hotel in Evry.



(i) The pictures n° 24 – 30 represent the moments of the *BrainVectors* sessions, i.e. the presentations of the coordinator (n° 24) and those of the other members of the consortium (n° 25-30)

(ii) The pictures n° 31 – 37 show some moments of the last session on April 3rd, where two projects, set up by two teams of attendees in the context of the *Project game*, were presented (photos n° 31 – 35), as well as those of the best poster and its author, who presented it (n° 35 – 37)..

Conferences


1


2

3


4

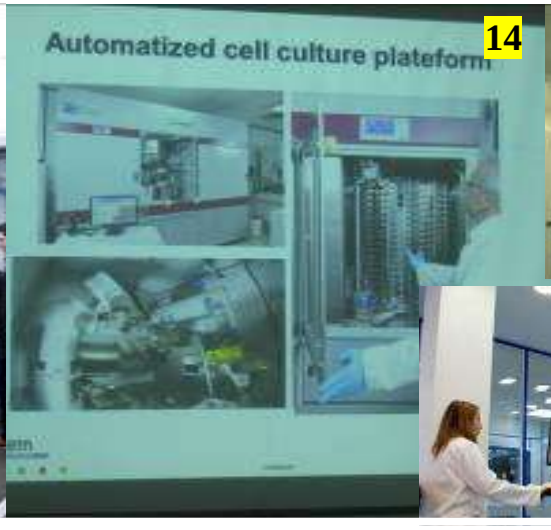

5

Poster viewing

Networking & social events

1: Visits of GENETHON & ISTEM

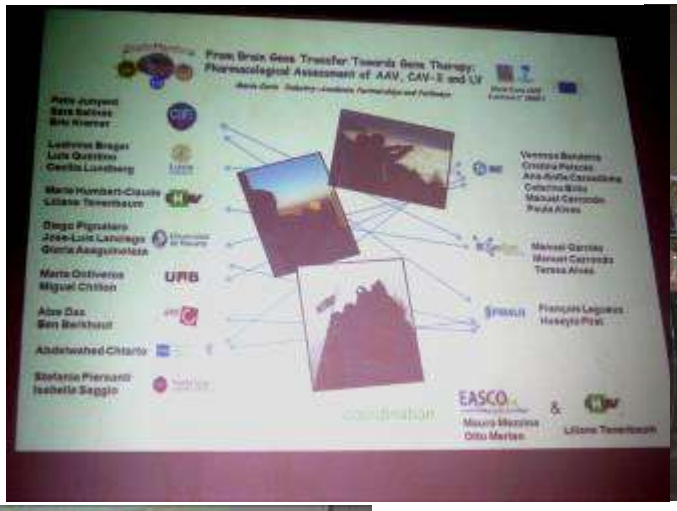
here is Genethon



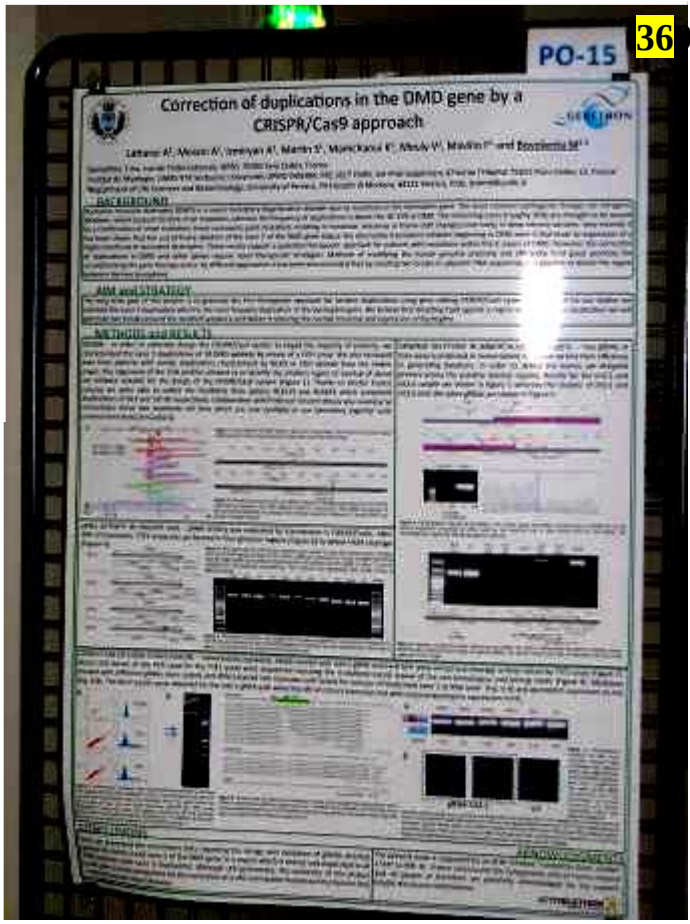
2:Visit of the Cathedral & Museum

3 : Cocktails and dinners

BrainVectors session



Project game & best poster



End of the workshop after this activity