

## I Brazilian Symposium on Transgenic Technology (1<sup>st</sup> BSTT) São Paulo, 10-12 March 2008

**João Bosco Pesquero**, Professor at the *Universidade Federal de São Paulo* (UNIFESP) and ISTT member, attended in 2007 the Transgenic Technology (TT) Meeting held in Brisbane, Australia, and there, he envisaged the idea to organise such an event in its country, Brazil, the fifth in surface and population among all countries on Earth. Together with **Heloisa Allegro Baptista** and their colleagues, they prepared and succeeded organising the First Brazilian Symposium on Transgenic Technology, gathering together international and national experts in the field of animal transgenesis. This conference received the support and co-sponsorship from the International Society for Transgenic Technologies (ISTT).



One of the first scientists invited at this meeting, Prof. **Oliver Smithies** (University of North Carolina at Chapel Hill, USA), readily accepted to participate and the Organisers became indebted and most grateful when he later was awarded the 2007 Nobel Prize in Physiology or Medicine, together with Mario Capecchi and Martin Evans, “for their discoveries of principles for introducing specific gene modifications in mice by the use of embryonic stem cells”, and generously maintained his compromise, attending this symposium in São

Paulo. Indeed, Oliver Smithies delivered an outstanding and very educative opening lecture by “turning pages” of his own laboratory notebooks thereby discussing the series of experiments reported on them that brought him to pioneer the modification of DNA molecules by homologous recombination in mammalian cells. He illustrated both successful experiments and failures and he concluded his delightful and touchy speech by recommending the students and young scientists that occupied all seats in the conference room to follow these three golden rules in Science: work hard, enjoy what you do and, most importantly, “keep good notes”.

After the keynote address, **Marcus Alexandre Finzi Corat** (UNICAMP, Brazil) introduced the audience with the basic techniques used for the generation of transgenic animals by gene addition and homologous recombination with a comprehensive lecture. **Andras Nagy** (Samuel Lunenfeld Research Institute, Mount Sinai Hospital, Toronto, Canada) followed next and focused his presentation on the power of ES-cell mediated genetics. In his talk, Andras Nagy reviewed the current status, similarities and different technical approaches of the various existing international consortiums aiming to knock-out each and every gene present in the mouse genome. He also discussed several updated and improved methodologies applied to ES cells aiming to tightly regulate the expression of genes by inducible systems (tetracycline) or to precisely rearrange genetic constructs at will and very reliably using site-specific recombinases (PhiC31).

**Lluís Montoliu** (CNB-CSIC, Madrid, Spain) delineated the limitations of standard transgenesis (i.e. position effects) and provided solutions to overcome them by using genomic-type transgenes, based on artificial chromosome-type constructs, usually resulting in predictable expression patterns in transgenic animals, according to that of the endogenous locus. **João Eduardo Krieger** (Inst. do Coração, INCOR, Brazil)

discussed the applications of lentivirus in transgenesis, for both mice and rats, introducing also the lentiviral transduction of male-germline stem cells and illustrated its use with examples of cardiovascular research.

Next session started with a presentation of the **ISTT**, by Lluís Montoliu, that included a remembrance of Prof. **Charles Babinet** (Institut Pasteur, Paris, France), ISTT Honorary Member and ISTT awarded scientist who unexpectedly had passed away one month before. This brief speech was followed by a most interesting talk by **Jean Louis Guénet** (Institut Pasteur, Paris, France) who discussed several examples of positional cloning of mouse mutations, from the initial mapping steps to the eventual gene identification. **Natalia Alenina** (Max-Delbrück-Center for Molecular Medicine, Berlin, Germany) shared her progress in spermatogonial cell-mediated gene transfer, on mice and rats. **Michael Bader** (Max-Delbrück-Center for Molecular Medicine, Berlin, Germany) summarised the technical achievements made in his lab over the years regarding all types of genetic modification in rats, also in cardiovascular research, highlighting the use of RNA interference approaches, because knock-down strategies could well complement the fact that no proper ES-cells have been reported, so far, in this rodent species.

**Denise Calisto Bongalhardo** (Instituto de Biologia, Universidade Federal de Pelotas, Brazil) nicely presented an overview of techniques applied for the production and use of transgenic birds, mostly chicken, and the associated applications for the preparation of recombinant proteins of interest in the egg, reporting also their progress and future plans in the field. The chicken presentation was followed by an interesting talk given by **Luciano Andrade Moreira** (CPqRR/FIOCRUZ-MG, Brazil) on the generation and potential use of transgenic mosquitoes, as a way to fight and help preventing the dissemination of infectious diseases transmitted by mosquitoes, such as malaria, through the interference with the parasite life cycle in the mosquito's digestive tract.



**Eduardo de Oliveira Melo** (CENARGEN, EMBRAPA, Brasilia) summarised the general aspects of cloning in mammals, presented in his talk the diverse types of nuclear transfer techniques and highlighted their progress and success in cloning bovine embryos, first achieved in Brazil in 2001. Next, **Elena Popova** (Max-Delbrück-Center for Molecular Medicine, Berlin, Germany) shared her very systematic and exhaustive approach towards cloning rats, as a potentially useful method to eventually achieve gene targeting in this rodent species that lacks properly-defined ES cells. However, in spite of the efforts presented, her results could not reproduce the published and to date unique success of cloned rats, reported in 2003. The search for alternative methods (i.e. iPS cells) to specifically target genes in rats appears to be the next obvious step.

The ethics in the use of transgenic animals was addressed by **Mirian Ghiraldini** (CEDEME, UNIFESP, Brazil), who presented the current Brazilian legislation in this topic

in a most comprehensive manner, calling the researchers to pay the required attention to the relevant issue of animal welfare. This presentation was followed by a talk on biosafety in animal experimentation and the need for adapting animal handling procedures to the new technologies. This talk was delivered by **Yara Barreira** (INSERM, Toulouse, France).

The last day of the symposium was devoted to applications of transgenic animals in biotechnology. The first lecture, delivered by **Louis Marie Houdebine** (INRA, Jouy en Josas, France) introduced the use of transgenic animals in biotechnology. He presented the benefits of using the mammary gland for bioreactor purposes, for the production of recombinant proteins, and compared the several mammalian species used in the field, that initially included sheep, pigs and cows but eventually have focused in goats and rabbits. He also summarised the current state-of-the-art regarding diverse transgenic animal projects that have been launched for the production of recombinant proteins of industrial or therapeutic interest, including the first approved product in Europe, by EMEA (2006), namely: human anti-thrombin III purified in the milk of transgenic goats produced by the biotech company GTC.

The use of transgenic fish as bioreactors was discussed by **Heden Luiz Marques Moreira** (*Universidade Federal de Pelotas, Brazil*), who described the particularities of the fish system and the attempts to use muscle or the seminal vesicle as a candidate target tissues to produce recombinant proteins of interest. The biotechnologically-oriented talks were continued with an example of non-rodent animal transgenesis in Brazil, presented by **Vicente Freitas** (*Universidade Estadual de Ceará, Fortaleza, Brazil*) who reported on the first successful transgenic goat produced in Brazil (named *Carlos*) carrying a transgene for the production of hG-CSF in their milk. This most



relevant work represented a multicentre collaboration effort that involved the initial generation of transgenic mice carrying the same construct, for functional validation purposes. The transgenic mice were produced at the *Laboratório de Animais Transgênicos* (UFRF, Rio de Janeiro, Brazil) and were presented in a poster in the symposium by **Luciene Paschoal Braga Dias**, who was chosen by the Selection Committee among the 20 Posters shown at the Symposium and received the best Poster award.

The meeting progressed with a presentation of transgenic mice producing clotting factor IX in their milk, a work presented by **Sharon Lisauskas** (CENARGEN, EMBRAPA, Brasilia), done in collaboration with the laboratory of the meeting organiser, João Bosco Pesquero, where the mice were initially generated. Next, the biomedical applications of RNA interference approaches were discussed by **Iscia Lopes-Cendes** (*Universidade Estadual de Campinas, Brazil*).

**Jean Louis Guénet** (Institut Pasteur, Paris, France) delivered a second talk on mouse functional genomics focused on top-down approaches, namely: gene driven

mutagenesis strategies (i.e. using the agent ENU) as an interesting alternative to the *in vitro* engineering of ES cells. The power of the method was illustrated by the fact that it can produce up to 10 different mutant alleles per gene, of all types, besides the classical null allele that is normally achieved via knockout standard methods, thereby increasing the chances to generate knowledge about the function of the gene and its relation with diseases.

In the last session of the meeting, **Ricardo Amaral Remer** (Atem&Remer, Brazil) discussed the issue of patenting the use of transgenic animals for defined purposes, according to the current Brazilian legislation, and encouraged his scientific colleagues to consider patenting their findings before publishing them, as a way to protect their potential industrial use and to further develop the national economy. **Alexandre Pontes** and **Emiliano Alves dos Santos Junior** (*Ministerio da Agricultura, Pecuária e Abastecimento*, MAPA, Brazil) introduced the *CODEX alimentarius* rules and the Brazilian current legislation in relation with the consumption of food produced in genetically modified animals.

This first Brazilian Symposium on Transgenic Technology was attended by more than 300 delegates from all over the country. Its success and impact in the Brazilian scientific community will see its outcome in the forthcoming years, since it is more than likely that new collaborative projects will emerge from networking interactions born or triggered by this conference. **João Bosco Pesquero** and **Heloisa Allegro Baptista**, along with the rest of members in the organizer committee,



have to be praised for a most successful and enjoyable meeting. This event is a milestone for the Brazilian Science that hopefully will continue in forthcoming editions of this symposium, and has already crystalized in the foundation of the *Sociedade Brasileira de Tecnologia Transgênica* (SBTT), a society created to support and disseminate the generation and use of genetically modified animals in Brazil.

### **Lluís Montoliu**

President of ISTT

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