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VRIJE UNIVERSITEIT BRUSSEL

PhD in Medical Sciences
2018-2019

INVITATION to the Public defence of

Prashant KADAM

To obtain the academic degree of **'DOCTOR OF MEDICAL SCIENCES'**

Spermatogonial stem cell transplantation: co-transplantation of supporting cells.

Thursday, 19 September 2019 at 5 p.m.
In Auditorium **Piet Brouwer**
Faculty of Medicine and Pharmacy, Laarbeeklaan 103, 1090 Brussel

How to reach the campus Jette:
http://www.vub.ac.be/english/infoabout/campuses

Summary of the dissertation

The transplantation of spermatogonial stem cells (SSCs) is a highly promising fertility restoration tool for former childhood cancer patients. However, the colonization efficiency of transplanted SSCs is low. Because mesenchymal stem cells (MSCs) have regenerative and cell supporting capacities, we hypothesized that (co-)transplanting MSCs might improve SSC transplantation efficiency. After developing an infertile mouse model which represented the clinical situation of infertility, we carried out four different transplantation strategies: (1) transplantation of SSCs (SSCT), transplantation of MSCs (MSCT), transplantation of both MSCs and SSCs (MS-SSCT), and transplantation of TGFß1-induced MSCs and SSCs (MSi-SSCT). The highest transplantation efficiency was obtained after MSi-SSCT. Moreover, even after injecting half the number of SSCs, the reproductive efficiency after MSi-SSCT was found to be similar to that after SSCT. Both SSCT and MSi-SSCT resulted in successful natural conception. Litter sizes were not different between MSi-SSCT and SSCT. Furthermore, we analyzed DNMT3A and H4K5ac expression patterns in both transplanted mice and their first-generation offspring. Compared to fertile controls, donor-derived germ cells showed lower expression levels of both DNMT3A and H4K5ac. However, the expression patterns were normal in the offspring. Since the expression levels of DNMT3A and H4K5ac were similar for SSCT and MSi-SSCT, we can assume that TGFß1-induced MSCs did not interfere with epigenetic modification.

From this thesis, the following conclusions could be drawn:

1- Co-transplanting TGFß1-induced MSCs improve SSC colonization efficiency in mice. TGFß1-treatment significantly lowers the expression of proteins playing a role in migration and, therefore, retracts MSCs in the testis where their paracrine contribution restores the testicular niche.

2- Co-transplanting SSCs and TGFß1-treated MSCs reach the reproductive potential of SSCT alone even after transplanting half the number of SSCs. Although lower expression of DNMT3A and H4K5ac were observed in donor-derived germ cells, normal levels were restored in offspring.

Curriculum Vitae

Prashant Kadam was born on 30th December 1985 in Patan (Maharashtra) India. In 2005, he started the study of Bachelor of Veterinary Sciences at the KNP College of Veterinary Science, MH, India. After graduation in 2010, he obtained a national fellowship for master in Animal Biotechnology at the National Dairy Research Institute, Karnal, India. After completing his master studies in 2012, he joined as a senior research fellow at Animal Biotechnology Center, Karnal, India. In 2014, he received a competitive international fellowship from the Indian Council of Agricultural Research to pursue his doctoral training under the supervision of Prof. Dr. Ellen Goossens at the Biology of the Testis lab of the Vrije Universiteit Brussel (VUB). His research focussed on improving the spermatogonial stem cell transplantation efficiency in a mouse model by co-transplanting mesenchymal stem cells. Prashant is an author of eight peer-reviewed publications, of which three as first author. Two additional manuscripts are currently in preparation. His work was presented at various national and international scientific conferences orally and by poster presentations.