Cancer Science Institute of Singapore

SEMINAR ANNOUNCEMENT

Daan Noordermeer

Group leader, Chromatin Dynamics group

Institute for Integrative Biology of the Cell (I2BC) - CNRS

CTCF Mediates Allele-specific Sub-TAD Organization at Paternally Imprinted Gene Loci

Date: **Tuesday, 21 Feb 2017**
Time: **11am – 12pm**
Venue: **#01-01B, Level 1, CeTM (MD6)** (14 Medical Drive, S117599)
Host: **Dr Touati Benoukraf**

Abstract:

Mammalian genes can be mono-allelicly expressed depending on their parental origin, a process called imprinting. Though only a relatively small number of genes are imprinted, this mechanism is of great importance for correct embryonic development. Imprinting is governed by allele-specific DNA methylation at defined Imprinting Control Regions (ICRs), which often influences the binding of the architectural CTCF protein. In collaboration with the group of Robert Feil (IGM-Montpellier, France) we have used a mix of allele-specific ChIP-seq, high-resolution 4C and microscopy to study how 3D chromatin organization is involved at the paternally imprinted Dlk1-Dio3 and Igf2-H19 loci. At both loci, the large majority of 3D interactions are containing within Topologically Associating Domain (TAD). Within these TADs dramatic allele-specific differences can be observed though. The maternal alleles form an invariant and more localized 3D structure that is demarcated by a mix of constitutive and multiple allele-specific CTCF binding sites. As such, these maternal specific sub-TADs encapsulate the ncRNA genes that are active on the maternal allele. In contrast, the paternal alleles adopt a more locus specific 3D organization. When active on the paternal allele, the Igf2 gene is contained within a sub-TAD with little specific internal structure and dynamics. In contrast, the imprinted protein-coding genes at the Dlk1-Dio3 locus co-occupy a large sub-TAD. Upon activation of these genes though, in neuronal cells, little changes in 3D organization are observed, suggesting this sub-TAD has a mostly constitutive structure. In conclusion, our study reveals that paternally imprinted gene loci in mammals are organized into allele-specific sub-TADs. Maternal alleles adopt the most structured and stable 3D organization, despite the imprint being present on the paternal allele. We hypothesize that imprinted gene expression at these loci relies most on the maternal 3D architecture, as supported by previous knock-out studies.

Biography:

Daan Noordermeer received his MSc in Biotechnology in 2003 from Wageningen University in the Netherlands. From 2004-2009, he did a PhD in Cell Biology at the Erasmus Medical Center in Rotterdam, the Netherlands, under the supervision of Wouter de Laat and Frank Grosveld. During his PhD, he studied how a regulatory element can autonomously influence chromatin structure and nuclear organization. His work confirmed that inter-chromosomal gene activation is possible in mammalian cells, but that this is rare and mostly determined by global genome structure (Noordermeer et al, Nature Cell Biology 2011). From 2009-2014, he did his postdoctoral work with Denis Duboule in the Swiss Cancer Institute (ISREC) at the Ecole Polytechnique Fédérale de Lausanne (EPFL). Here, he studied how 3D organization of chromatin is involved in collinear activation of Hox-genes. He showed, for the first time, that domains of histone modifications in mammals adopt specialized and dynamic spatial configurations (Noordermeer et al, Science 2011, Noordermeer et al, eLife 2014, Vieux-Rochas et al, PNAS 2015). In 2014, Daan Noordermeer was recruited as a group leader at the Institute for Integrative Biology of the Cell (I2BC) in Gif-sur-Yvette (France) and as a tenured scientist by the French National Centre for Scientific Research (CNRS). He leads chromatin dynamics team that studies the structural and functional links between epigenetic domains, the function of insulator proteins and the 3D compartmentalization of chromatin. Moreover, the team develops new technology to study 3D genome organization at ultra-high resolution in individual cells. Daan Noordermeer has won multiple prizes for his scientific work (Prix Coups d'Elan Pour La Recherche Française – 2015 and Junior Debiopharm Group Life-Sciences Award – 2012) and his work has appeared in high profile journals like Science, Nature, Nature Cell Biology, PLOS Biology and PNAS.