INSTITUTO BIOMEDICINA Y BIOTECNOLOGIA DE CANTABRIA

Developmental Biology Laboratory of Dr. Marian Ros

(http://www.biodes.unican.es)

Regulation of gene expression during development

Searching for an **FPU** candidate - To develop a PhD Thesis investigating the involvement of Sp6 and Sp8 transcription factors in the pathogenesis of the Split Hand Foot Malformation.

Split Hand Foot Malformation (HFM) is a malformation of the hand and/or foot characterized by the loss or deformity of the central digits that leads to a central cleft and the subsequent split appearance. Six loci have so far been identified for SHFM but despite the genetic heterogeneity, a convergence towards the Tp63 network can be appreciated. TP63 is a member of the p53 family of TFs that plays multiple functions including control of skin stratification and adult stem/progenitor cell regulation. TP63, responsible of one of the SHFM types, and studies in our laboratory and by others indicate that most types of SHFM are due to defects in the TP63 network directing *Fgf8* expression. FGF8 is the growth factor responsible for the action of the Apical Ectodermal Ridge (AER) a signalling centre absolutely necessary for limb development.

Sp6 and Sp8 are two members of the Sp family of transcription factors that control, in a redundant and dose dependent manner, Fgf8 activation. Most interesting, a significant reduction in *Sp6/Sp8* gene dosage phenocopies the human SHFM phenotype. Since similar phenotypes are frequently caused by disruption of different components of a regulatory network, it seems reasonable to consider that Sp6/Sp8 participate in the Tp63 network. To check this hypothesis we have generated *Sp8:FLAG* knock-in allele and identified the genetic network in which SP8 participates by Chip-seq and RNA-seq. To further check our hypothesis our aim is to generate an *Sp6:FLAG* knock-in allele and to investigate the genetic interaction between *Sp* genes and the other SHFM causative genes.

The research is highly multidisciplinary and integrative and uses transcriptomics and epigenomics analysis, Chip-seq, CRISPR and classical developmental genetics approaches. Our aim is to understand the mechanisms responsible for morphogenesis at cellular, molecular and genetic levels in both health and disease.

The IBBTEC (http://web.unican.es/ibbtec/Paginas/default.aspx) is a new research institute of the CSIC, University of Cantabria and SODERCAN. It is located in the Scientific and Technologic Park of Santander and provides an enthusiastic and supportive environment with state-of-the-art research facilities.

Contact Marian Ros (rosm@unican.es)

Selected publications:

- Roselló, A., Ros M.A. and Torres, M. (2011) *Science* 332:1086-1088
- Cooper, K.L., Hu, J. K-H, ten Berge, D., Fernandez-Teran, M., Ros M.A. and Tabin, C.J. (2011) *Science* 332:1083-1086.
- Sheth R, Marcon L, Bastida MF, Junco M, Quintana L, Dahn R, Kmita M, Sharpe J, Ros M. (2012) *Science* 338(6113):1476-80
- Haro E, Delgado I, Junco M, Yamada Y, Mansouri A, Oberg KC, Ros MA. (2014) *PLoS Genet.* Aug 28;10(8):e1004468
- Saiz-Lopez P, Chinnaiya K, Campa VM, Delgado I, Ros* MA, Towers* M (2015) *Nat Commun.* Sep 18;6:8108.
- Ros MA (2016) *Genes Dev*. 30(10):1135-7.
- Saiz-Lopez P, Chinnaiya K, Towers M, Ros MA, (2017) *Development* 144(3):479-486.
- Pickering J, Rich CA, Stainton H, Aceituno C, Chinnaiya K, Saiz-Lopez P, Ros MA, Towers M. Elife. 2018 Sep 3;7. pii: e37429.