ESR1Project: Identification of Sox6 and NR2F2 downstream networks controlling normal (and malignant) erythropoiesis.

The successive waves of erythropoiesis during development produce different hemoglobins, in order to meet the oxygenation need of the developing embryo.

The transition from fetal ($\alpha 2\gamma 2$) to adult ($\alpha 2\beta 2$) hemoglobin –the Hemoglobin Switching- is of major clinical interest[1]. In fact, the persistence of fetal hemoglobin throughout life (HPFH), when co-inherited with β-hemoglobinopathies, greatly reduces their severity. Thus, the understanding of the molecular mechanisms controlling the hemoglobin switching is essential to design new therapies aimed to reactivate fetal hemoglobin in patients with β-hemoglobinopathies (the most common genetic disease worldwide). So far, some of the involved transcription factors have been identified, including Bcl11aXL, Sox6, LRF, Tr2/Tr4 and NR2F2/Coup-TFII itself, but their interplay is unclear.

In this context, our laboratory is interested in the characterization of transcription factors regulating the differential expression of embryo/fetal versus adult globins genes. The specific aim of this project is to better characterize the functional role of the transcription factor NR2F2[2], expressed in in early hematopoieisis and of Sox6[3], expressed in adult erythroid cells, and of their downstream networks. We use molecular and cellular biology approaches, including chromatin immunoprecipitation, Flow Cytometry, lentiviral-mediated overexpression and CRISPR/Cas9-mediated knockout in cell lines and in *ex-vivo* cell cultures from transgenic mouse models.

References

1) Sankaran VG. et al. Advances in the understanding of haemoglobin switching. Br J Haematol. 2010, 149:181-94.

2) Lin FJ et al. Coup d'Etat: an orphan takes control. Endocr. Rev. 2011, 32:404-21.

3) Barbarani G et al. SOX6 blocks the proliferation of BCR-ABL1(+) and JAK2V617F(+) leukemic cells. Sci Rep. 2019, 9:3388.