

Speaker name: Andrés Aguilera, University of Seville

Title: “RNA-mediated genome instability”

Short abstract:

Nascent RNA can form co-transcriptional RNA-DNA hybrids or R loops, which may play an important physiological role in transcription regulation but can also be a source of replication stress and genome instability, hallmarks of cancer cells. A number of transcription and RNA processing and export factors play collateral roles in preventing the accumulation of RNA-DNA hybrids that may become harmful for the cell. These include the THO complex and Senataxin, key players in preventing R loop accumulation, as well as other RNA-binding proteins such as SRSF1, Npl3, Yra1/ALY and a number of RNA helicases. Depletion of many of these factors leads to R loop-dependent genome instability that is accompanied by an alteration in the pattern of replication. To get further insight into the connection between RNA biogenesis and genome dynamics, we identified new human proteins that could transiently interact with human THOC1 and others controlling RNA-DNA hybrid accumulation. Among them, we identified histone deacetylases and splicing factors, whose depletion lead to different types of genetic instability. With the aim at understanding the putative role of these proteins in RNA-DNA hybrid formation and the maintenance of genome integrity, we carried out a detailed characterization of their functional interconnection with replication stress in nucleus and mitochondria, that is adding new insights into the role of RNA in genome dynamics.

Short bio:

Andrés Aguilera is Professor of Genetics of the University of Seville and Director of the Andalusian Centre of Molecular Biology and Regenerative Medicine (CABIMER). He obtained his PhD in Seville in 1983. After two postdoctoral stays in the Darmstadt Technical University (Germany) and the NYU Medical Center (USA), he started his own lab dedicated to Genome Instability in 1991 in the Faculty of Biology (Univ. Seville), and since 2006 in CABIMER. His research led to the identification of the THO complex and its function in mRNP biogenesis and R loop prevention and the role of co-transcriptional R loops in genome instability and their connection with chromatin modifications, and has largely contributed to understand the mechanisms by which transcription and RNA cause replication stress and genome instability and the mechanisms of DSB repair by sister chromatid recombination. Member of EMBO, he belongs to the International Scientific Advisory Boards of different Research Centres and to the Editorial Board of several scientific journals. Holder of several national scientific prizes and distinctions in Spain, like the Carmen & Severo Ochoa National Prize on Molecular Biology, he has been awarded HFSP and ERCAdv grants, among other international programmes.

Link lab website: <http://www.cabimer.es/web3/en/research-groups/genome-instability-cancer/>