Generating animal models by genetic manipulation

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Our laboratory is interested in understanding the underlying pathological mechanisms that result in a group of human rare diseases globally known as albinism, a heterogeneous genetic condition associated with mutations in at least 20 genes, visual impairment, and often with pigmentation alterations. These research projects on human rare diseases are carried out within our participation in the CIBERER-ISCIII.

We have generated and analysed new animal models to study visual abnormalities that affect retina development associated with albinism and other retinopathies, such as achromatopsia. Using mouse models, we have explored the use of small molecules as potential therapeutic candidates for albinism. In collaboration with Angel Carracedo (University of Santiago de Compostela) and Carmen Ayuso (University Hospital Jiménez Díaz Foundation), within the CIBERER-ISCIII, we devised a proposal for the universal genetic diagnosis of all known mutations in albinism, which we are applying in cooperation with ALBA, the Spanish association in support of people with albinism. We also launched the Albino Day initiative for the first time in Spain, a date in hospital when patients with albinism are explored by experts specialized in this rare genetic condition.

We are also interested in understanding the function of regulatory elements necessary to identify gene expression domains in mammalian genomes and that contribute to specify their expression pattern in space and time. The mouse tyrosinase locus, used as experimental model, has helped us identify genome boundaries or insulators that protect it from surrounding genes. In transgenic animals –zebrafish and mice— we use different types of gene constructs to study the relevance of specific sequences. The functional analysis of regulatory elements within the intergenic sequences can be now addressed more efficiently, thanks to the new CRISPR-Cas9 gene modification system, whose application in mice we pioneered in Spain and implemented successfully in our laboratory.

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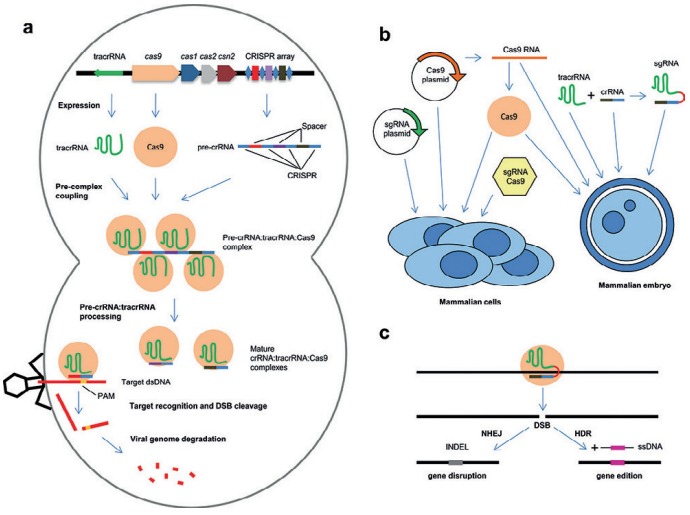

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The natural bacterial CRISPR-Cas system for defence against viruses (a) and derived genome editing tools in mammalian cells (b, c) (from Mojica FJM and Montoliu L, 2016).

SELECTED PUBLICATIONS

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