GENERATION OF THE RING14 MOUSE MODEL TO BETTER UNDERSTAND THE PATHOPHYSIOLOGY OF THE HUMAN SYNDROME

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SUBMITTED TO PEER REVIEW PROCESS WITH INTERNATIONAL BOARD

ABSTRACT

Broad objectives and specific aims: RING14 is a very rare human genetic syndrome that induces a large number of features affecting behavior and cognition, locomotor activity, epilepsy and morphology.

Background/Rationale: Further understanding of the RING14 syndrome will need the development of an animal model. The mouse, with a very high conservation of gene sequence and function with human, represents the most used animal model for fundamental and applied research. In addition the mouse genetic toolbox offers a wide range of technics, including chromosomal engineering and cellular markers.

Research design and methods for achieving the stated objectives: The project will focus on the making of a mouse model with rearrangements of the homologous region to human chromosome 14 located on the telomeric part of mouse chromosome 12. We will use embryonic stem cells to engineer rearrangement within the mouse chromosome 12 and introduce a series of markers so that a ring could be induced and followed.

Anticipated output: The RING14 mouse model will be analyzed to better understand the transmission of the ring chromosome in mutant cells, to check the viability of the cells containing the RING14 chromosome, to carry a comprehensive and standardized phenotypic analysis of the syndrome, to compare the phenotypic assessment in the mouse and in human patients, to identify the gene(s) and the pathways altered in RING14 and finally to propose and eventually test therapeutic approaches.