**Behavior analysis of RSK2 deficient mice:**
**An animal model for the cognitive impairment In the Coffin-Lowry syndrome**

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We have shown that mutations in the RSK2 gene in human leads either to the Coffin-Lowry syndrome, i.e., mental retardation associated with characteristic physical features, or to a form of X-linked non specific mental retardation (XLMR). RSK2 is a member of the p90 ribosomal S6 kinases (RSK) which are serine-threonine mitogen-activated protein kinases acting in the RAS/MAPK signal transduction pathway. To understand how the lack of RSK2 protein could be involved in cognitive functions, we generated a targeted null mutation in the murine homologous gene. The mutant mice are viable, with no obvious physical abnormalities. and no motor disorders were observed.
Wild type and mutants did not differ in emotional or exploratory behavior and motor coordination as measured in open field, elevated o-maze, dark and light box and rotarod. RSK2 deficient mice were also subjected to different tests of memory and learning. Thus far, results in the eight-arm radial maze (spatial working memory) indicate that mutant mice perform barely above chance level in choosing correctly consecutive arms. Likewise, mutant mice were impaired, in comparison to littermates, in a matching-to-place (DMP) version of the Morris Water maze in which they had to learn sequentially five different platform positions.
These results suggest a role of the RSK2 protein in cognitive functions in mice that resemble some of the deficits observed in humans. Thus, this mutant mouse appears to be a promising model to analyze the causes of the mental retardation component of human syndromes.

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