Back to The Rat!

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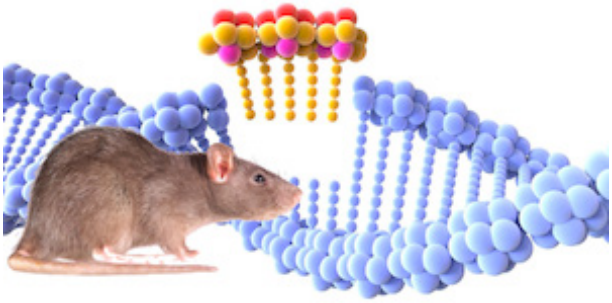
For the last three decades of the 20th century, rats were the kings of biomedical research, particularly in cardiovascular and behavioral neuroscience studies. Then genome engineering arrived, and mice took the throne. In the early 1980s, it was indeed easier to develop transgenic mice than rats, mainly due to the difficulty to generate germline-competent rat embryonic stem (ES) cells. It is no surprise, then, that when the first transgenic mouse model was generated, in 1981, no constitutive or conditional gene Knockout, Knockin, or site-specific mutagenesis in rats was available yet. It took nine more years for the first transgenic rat to finally come to light, thanks to the development of other techniques not involving direct manipulation of ES cells, including antisense RNA, RNA interference, and chemical mutagenesis.[1]

However, the real "rat revolution" occurred when CRISPR/Cas9 made its appearance in 2012, allowing scientists to target any sequence directly in mammalian zygotes, thus eliminating the lengthy process of ES cell manipulation required to generate transgenic animals through classical homologous recombination techniques. Since then, a great number of rat models have been developed for a wide variety of research areas, especially where rat's intrinsic characteristics makes it the model of choice.[2]



For example, rats provide excellent animal models to study drug metabolism and pharmacokinetics, as well as cardiovascular, neurological, and metabolic diseases: their size (rats are 10 times bigger than mice) allows multiple sampling of larger tissue volumes, more precise injection of compounds into the brain, and easier microsurgery.[1,3,4] The rat also represents a key model organism in behavioral neuroscience, as it is much more social than the mouse, and its behavior resembles very much that of humans. Finally, rats serve as useful tools to unveil the role of genes that are present in humans but absent in mice, including genes involved in immunity and production of pheromones.[5]

Rats have therefore regained the place of honor that was rightfully theirs, returning to the forefront of biomedical studies, especially in certain areas of investigation. Accordingly, researchers can choose the most appropriate model, whether it is mouse or rat, based on the biology and the particular process or gene being studied, rather than being limited by technical issues.

References:

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