Animal Model

PARP1 -/- mice: an animal model for cancer, autoimmune encephalomyelitis, arthritis and diabetes

Reference Number 11-00041

Abstract

Challenge

Poly(ADP-ribose) polymerase-1 (PARP-1) catalyzes the modification of nuclear enzymes by (ADP-ribosyl)ation. PARP-1 function was first associated with DNA single-stranded break repair, especially in tumor cells, and maintenance of genomic integrity. Accumulating evidence suggests that PARP-1 also plays important roles in other disease processes, like central nervous system dysfunctions (e.g. Stroke, Parkinson), carcinogenesis and autoimmune diseases such as type I diabetes[1,2]. Therefore, several studies have examined PARP-1 as a target for therapeutic interventions[3]. In particular, cancer types with reduced or deficient DNA repair via homologous recombination are highly vulnerable to PARP-1 inhibitors, with the PARP-1 axis remaining the only repair system available. PARP-1 inhibitors causing selective death of such cancer cells are currently under investigation in clinical trials[4].

Technology

The technology provides mice deficient in PARP-1. In PARP-1 -/- mice, profound changes in the activity of transcription factors such as nuclear factor-?B (NF?B) and nuclear factor of activated T cells (NFAT) can be observed. The phenotype of these knockout mice is reflected by an altered immune response due to dysfunctional PARP-1 regulation of transcriptional networks involved in immune cell activation and inflammatory cytokine production. Also T cell dependent antibody responses have been reported to be reduced in PARP-1-/- mice. Administration of PARP-1 inhibitors in animal disease models has been shown to ameliorate clinical signs of experimental autoimmune encephalomyelitis, arthritis, diabetes and cancer. Especially as the specificity of these inhibitors has not been completely examined for all diseases, PARP-1-/- mice offer a valuable tool for studies of the activity and specificity of PARP-1 inhibitors for the treatment of cancer and other PARP-1-associated diseases.

Commercial Opportunity

Breeding pairs of PARP $1^{-/-}$ mice are available under Tangible Property Licence Agreement.

Further Reading

- [1] Tong et al. Biochim Biophys Acta 2001; 1552(1): 27-37
- [2] Hassa & Hottiger, Front Biosci 2008; 13: 3046-3082
- [3] Fauzee et al, Pathol Oncol Res 2010; 16(4):469-478
- [4] Iglehart & Silver, N Engl J Med 2010; 361(2): 189-191

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