

## **Immunosuppression of Rat Myasthenia Gravis by Oral Administration of a Syngeneic Recombinant Acetylcholine Receptor Fragment**

Prasanta K Maiti<sup>\*</sup>, Tali Feferman<sup>\*</sup>, Sin-Hyeog Im<sup>\*</sup>, Miriam C Souroujon<sup>\*†</sup>, and Sara Fuchs<sup>\*</sup>

<sup>\*</sup>Department of Immunology, Weizmann Institute of Science, Rehovot 76100, Israel and

<sup>†</sup>The Open University of Israel, Tel Aviv 61392, Israel.

Induction of immunological tolerance by mucosal administration of antigen is an attractive strategy for prevention or treatment of illness resulting from untoward inflammatory immune reactions against self- or non-self-antigens. We have investigated the feasibility of suppressing ongoing experimental autoimmune myasthenia gravis (EAMG) in rats by a *syngeneic* rat recombinant fragment, corresponding to the extracellular domain of the acetylcholine receptor (AChR)  $\alpha$ -subunit (R $\alpha$ 1-205). Oral administration of the *syngeneic* R $\alpha$ 1-205 led to suppression of EAMG when initiated at the acute or at the chronic phase of the disease. The underlying mechanism of the therapeutic effect of the *syngeneic* fragment appears to be by a shift in immune regulation from Th1 to Th2 as evidenced by downregulated mRNA expression levels of IFN- $\gamma$  and TNF- $\alpha$  and upregulated levels of IL-10 in treated rats. Isotype analysis of anti-AChR antibodies consolidated this finding. Analyses of the expression levels of co-stimulatory factors revealed an impaired Th1 signaling pathway via CD28/CTLA-4:B7.1. R $\alpha$ 1-205 does not induce elevation in TGF- $\beta$  and elicitation of autoregulatory cells that can passively transfer the suppression of EAMG. In conclusion, the ability to suppress EAMG by a non-immunogenic *syngeneic* fragment of AChR is encouraging and may in future be considered for the treatment of MG in humans.