

INTERMEDIILYSIN-MEDIATED CELL ABLATION IN THE RAT AND ZEBRAFISH

Marina McCoy Hanson

Elizabeth Bryda, Dissertation Supervisor

ABSTRACT

Current methodologies of cell ablation have limitations with respect to the types of cells that can be targeted, the lack of specificity of ablation and the lack of appropriate methodologies to facilitate their use across species. The goal of our study is to provide proof of concept that intermedilysin (ILY) administration to ablate cells expressing human CD59 (hCD59) provides a sensitive, specific, and versatile tool for cell ablation in rats and zebrafish. While effective cell ablation using this system has been demonstrated previously in mice, it has not been tested in other model organisms. We generated a new transgenic rat line to study hemolytic anemia which expresses hCD59 specifically on erythrocytes rendering them susceptible to lysis by administration of the otherwise inert bacterial toxin, ILY. ILY intravenous injection dramatically reduced hematocrit within 10 minutes, with no effect on wild type rats. To test ablation of cell types within whole organs, we have generated a fluorescent protein-tagged hCD59 which can be expressed constitutively in multiple cell types, including tyrosine-hydroxylase (TH)-expressing neurons, when Cre recombinase is present. Such models can be useful for study of neurodegenerative disorders, such as Parkinson's disease. When rats were dosed with ILY, there was a decrease in TH-positive neurons. To demonstrate applicability in non-rodent models, we are testing the efficacy of the hCD59-ILY system in zebrafish. Ongoing studies aim to validate the hCD59-ILY system by production of transgenic zebrafish which express hCD59 in motor neurons. The use of hCD59-ILY will have wide application for any studies in any species that can benefit from selective cell ablation *in vivo*.