

## Gregory A. Grabowski, MD

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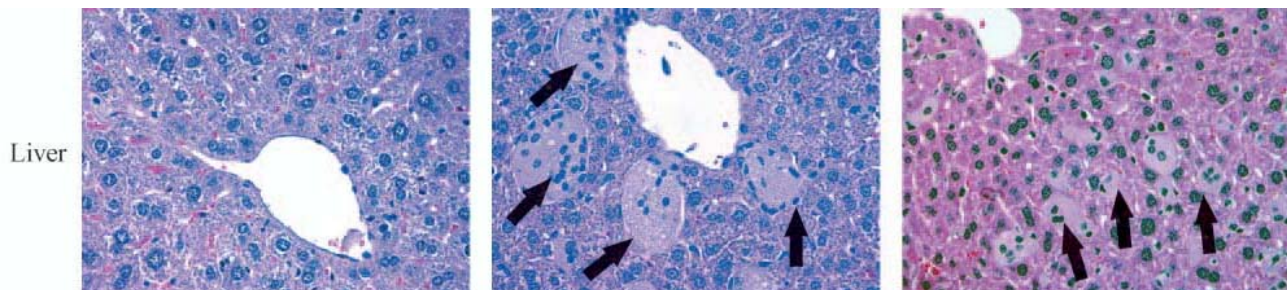
### Description of Research:

Dr. Grabowski investigates the pathogenesis of selected lysosomal storage diseases. Studies range from gene transfer, purification and characterization of recombinantly produced selectively mutated enzymes, knock-in and knock-out mouse generation, and genome wide studies of transcriptomes and proteomes. These studies use high-density **microarrays and bioinformatics** to identify molecular signatures of lysosome-based biological processes, and **integrative morphology** to define the cellular basis of molecular signatures and the phenotype of organs of the digestive system in gene-targeted mice. The overall goal of his research program is to define the nature of the signature pathways in disease pathogenesis, and the evolution of the disease phenotypes in mouse models that have been developed as prototypes for selected human diseases. By combining biochemistry/molecular genetics, high-throughput functional genomics, and histopathologic approaches, new strategies will be developed for effective therapeutic interventions and their evaluation by novel biomarkers. Particular emphasis relates to the regulatory role of macrophages or the tissue-specific injury of the liver, spleen and intestine, and the molecular signals controlling the process.

### Collaborations:

Dr. Grabowski has used the **Microarray and Bioinformatics Cores** in collaboration with Dr. Aronow to identify the signature pathways in the pathogenesis of a mouse model of Gaucher Disease. He also works with Dr. Witte and uses the **Integrative Morphology Core** examining the supplementation of lysosomal acid lipase in a mouse model of atherosclerosis.

### Representative Figure:



Storage cells in the liver of 22-week old PS-NA (mice expressing low levels of prosaposin and saposins), 4L/PS-NA (V394L point mutation of acid beta-glucosidase backcrossed with PS-NA mice), and 9H/PS-NA (D409H point mutation of acid beta-glucosidase backcrossed with PS-NA mice) mice. PS-NA livers had a normal appearance, while clusters of lipid storage cells (arrows) were observed in 4L/PS-NA and 9H/PS-NA livers. Fig. 2 from J Lipid Res, 2005; 46: 2102-13.