

BTP Summer Internship 2017

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Enzyvant

- Biotech with focus on developing treatments for rare diseases
- Two main pipelines for rare genetic diseases:
 - Complete Digeorge Syndrome
 - Large deletion in chromosome 22 leads to immunodeficiency
 - Est. 1/4000 people
 - RVT-802 through phase 3 clinical trials
 - **Farber Disease**
 - Acid ceramidase deficiency
 - Est. 80 cases reported worldwide
 - RVT-801 in pre-clinical studies
- RVT-801 research with Dr. Edward Schuchman in NYC



Acid Ceramidase (AC) Deficiency

- Mutations in human *ASAH1* gene
 - Loss of acid ceramidase activity in lysosomes
- Leads to two distinct diseases
 - Farber disease
 - Lysosomal storage disease
 - Average lifespan = 2 years
 - Spinal Muscular Atrophy with Progressive Myoclonic Epilepsy (SMA-PDE)
 - Molecular mechanisms not fully understood
 - Patients live into late teens
- Enzyvant RVT-801 in preclinical studies for treatment of Farber disease
 - Enzyme replacement therapy (ERT)
 - Initial mouse studies show increased lifespan, reduction of ceramide buildup
 - No known structure of acid ceramidase



medicalrealm.net

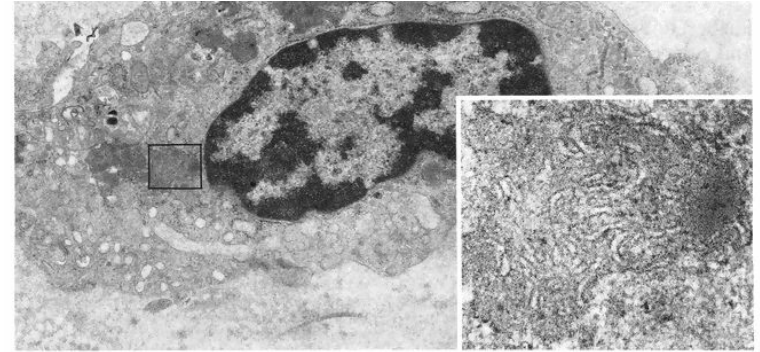
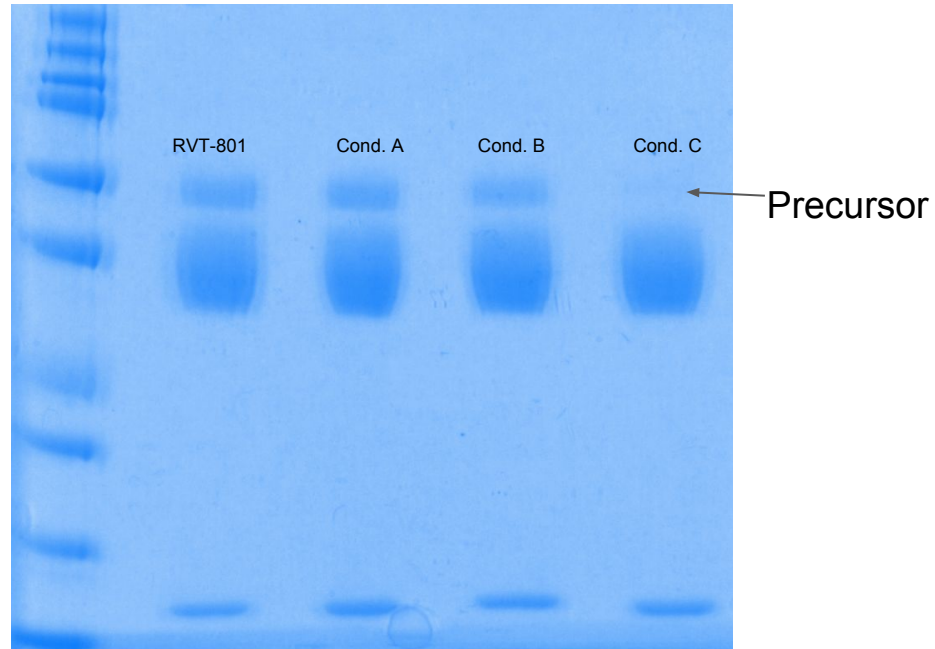


Fig. 1. A macrophage in a subcutaneous nodule from a patient with Farber disease, with a cytoplasmic inclusion body containing Farber bodies. $\times 19000$ Inset: $\times 100000$

Koga, M., Ishihara, T., Uchino, F., Virchows Archiv. 1992, 62, 297-302.

Summer Internship Research with RVT-801

- Study how RVT-801 (rhAC) responded to different treatments
 - Deglycosylation
 - Activity vs. pH
 - Enzymatic precursor processing
- Collaboration with Dr. Schuchman to solve crystal structure of AC
 - RVT-801 is a mixture of precursor and active form of AC
 - Learned during internship how to convert most of precursor AC to active form
 - Could prove valuable in crystallography trials



Internship Experience

- Small research group consisting of Dr. Schuchman, two senior researchers and three research assistants/technicians
- Most of the research focus was on the preclinical studies of the effect of rhAC in Farber disease mouse models
 - Very interesting/exciting to see these experiments and learn about the process of testing a potential enzyme replacement molecule before it could go into clinical trials!
 - Slight delay to set up biophysical/biochemical experiments on rhAC
 - More independence to set these up rather than shadow someone on their own experiments
- Rigid daily schedule and frequent group progress meetings
- All reagents/buffers/gels from commercial sources
- Day to day research similar to some academic settings in this smaller group as opposed to work in a very large company setting

Advice for BTP Members

- Reach out to collaborators and colleagues for internship ideas
 - Our collaboration led directly to this opportunity, made the entire process much easier!
- Search for biotechs doing research in a similar area to your lab work
 - Don't be afraid to contact them directly, even if there are no obvious internship listings
 - If not in your research area, find something that interests you/learn a new technique you are interested in!
- Housing, housing housing!
 - Can be very difficult and time consuming to secure in larger cities
 - Search **early** and often!
 - Search for organizations that may host interns/students/young professionals
 - Other universities often have open summer housing for interns
 - This saved me a lot of money, time and hassle
- The internship is a very valuable learning experience!
 - A chance to do exciting research and learn new techniques!
 - Make new connections in biotech!
 - Break from lab bench work = time to reflect on your progress and focus your future directions
 - A chance to experience a new place for several months!

Acknowledgments

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- BTP
- Dr. Garman and our lab
- MCB

