Poster ID: 90

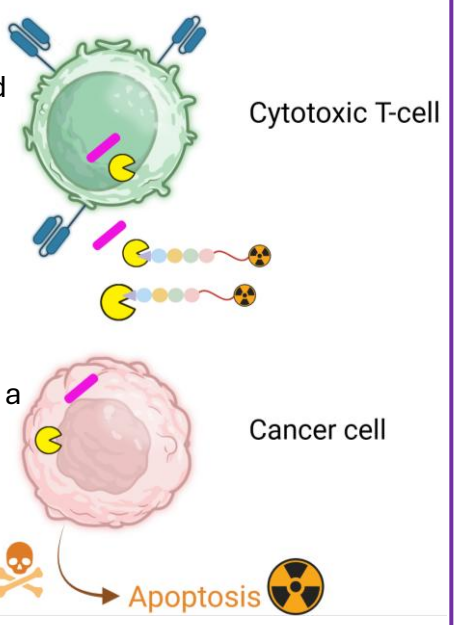
Novel Granzyme B inhibitors for early cancer treatment response measurement via PET

Magdalini Thanopoulou[1], N. Shikut[1], E. Verhulst[2],, M. Berg[3], C. Kersten[4], T. Schirmeister[4], F. Elvas[5] R. Pacifico[1], I. de Meester[2], P. Van Der Veken[1]

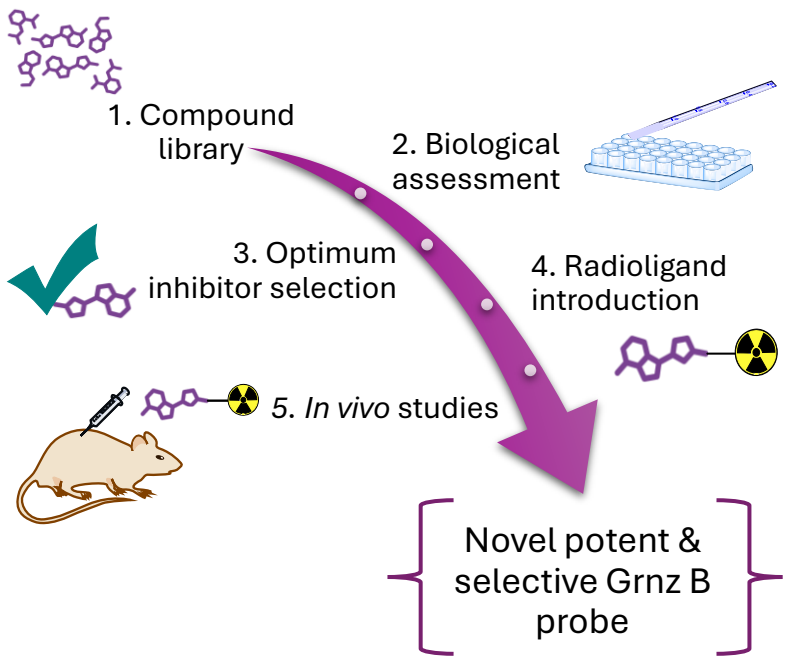
[1]Laboratory of Medicinal Chemistry, Department of Pharmaceutical Sciences, University of Antwerp, Antwerp, Belgium
[2]Laboratory of Medicinal Biochemistry, Department of Pharmaceutical Sciences, University of Antwerp, Antwerp, Belgium
[3]Infla-med Center of Excellence, University of Antwerp, Belgium
[4]Institute of Pharmaceutical and Biomedical Sciences, Johannes Gutenberg University, Mainz, Germany
[5]Molecular Imaging and Radiology, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium

Introduction

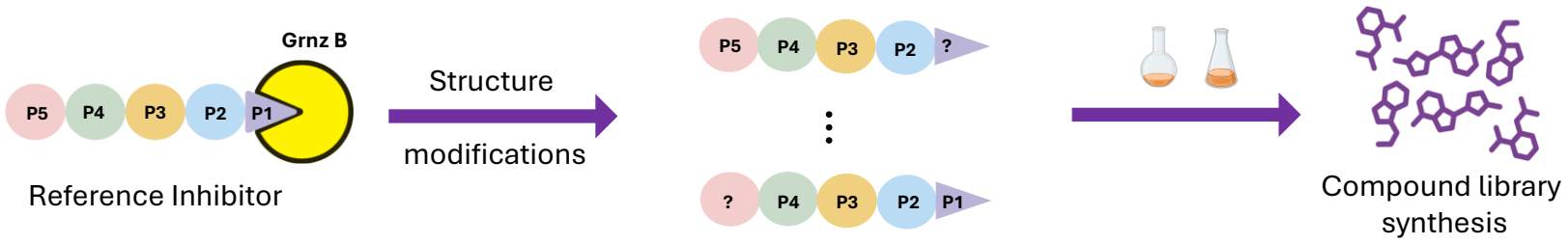
- **Granzyme B (Grnz B)** is **a serine protease** secreted **by cytotoxic T lymphocytes (CTL)** and natural killer (NK) cells to target pathogen infected and **cancer cells.**[1]
- Targeting Grnz B provides a **direct window to cancer treatment response.**[1]



Aims & Objectives



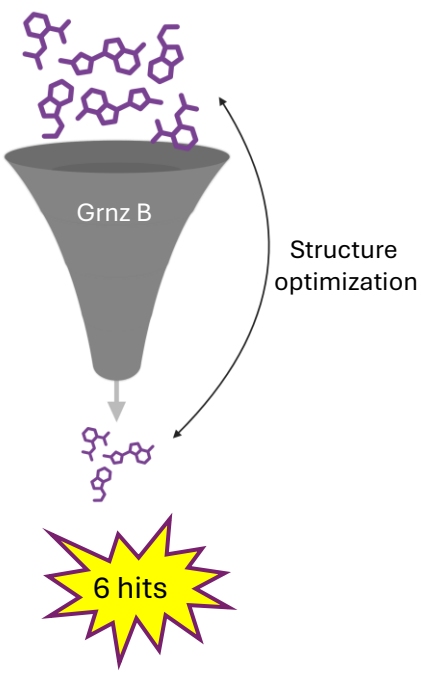
1. Compound Library Synthesis



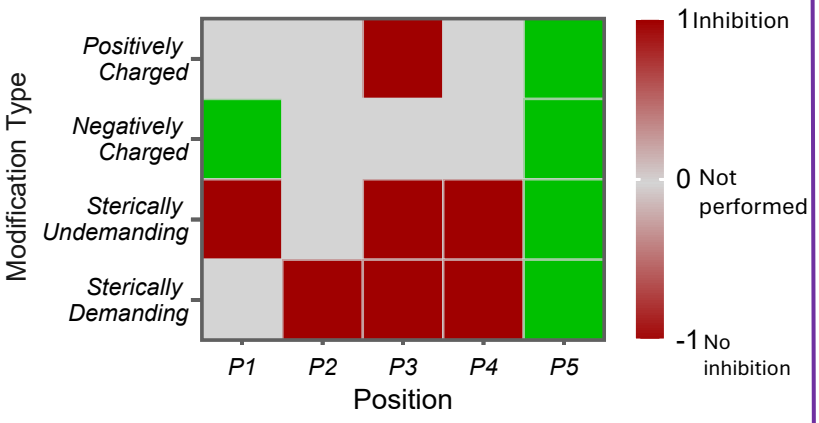
2. *In vitro* Biological Evaluation

A. Grnz B Screening

42 compounds



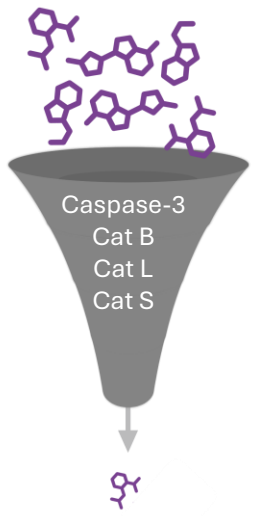
B. SAR Study



- ✓**P1** requires a **negatively** charged moiety
- ✓**P5** modifications are **well-tolerated**
- ✓**Low/no** tolerance in the **P2 – P4** modifications

C. Off-target Screening

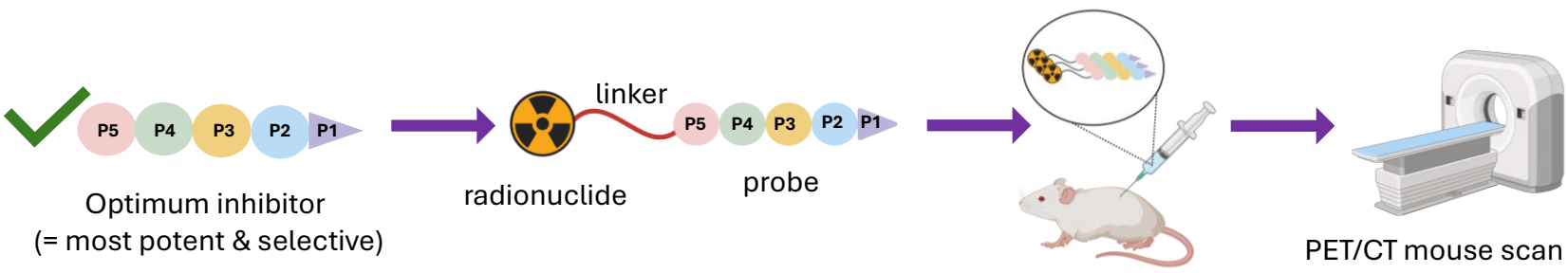
77 compounds



1 hit against Cat S

Selectivity

3. *In vivo* Evaluation – Future Work



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[1]Scott, J. I. et al. *Chem. Int. Ed.* 2021, 60 **(11)**, 5699–5703

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