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

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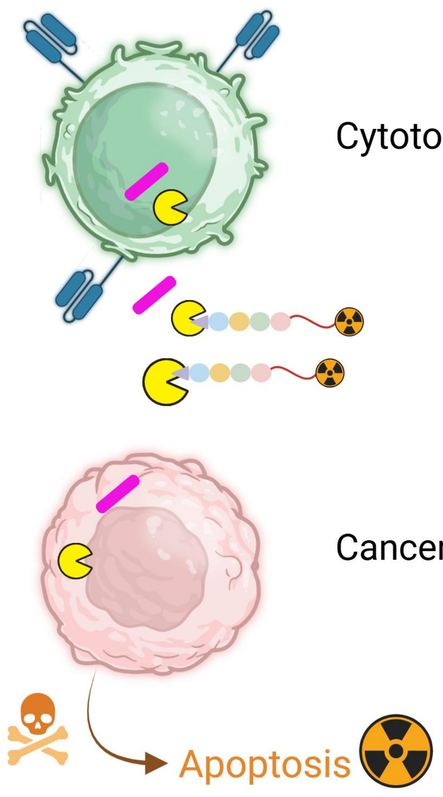
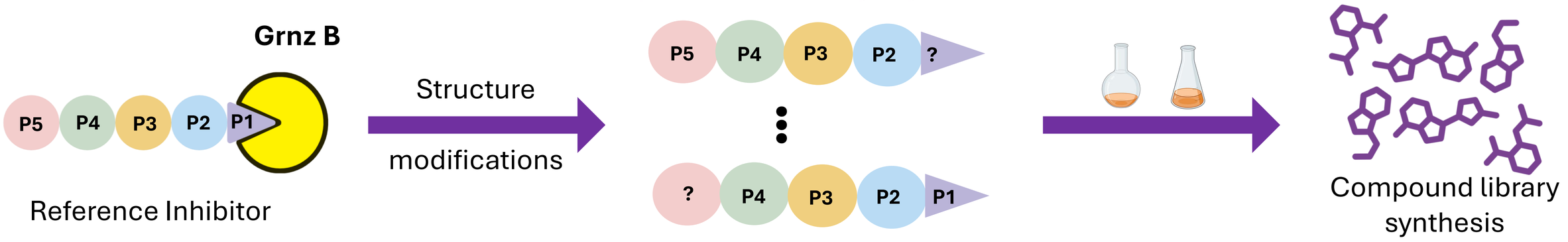
Introduction

- **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]



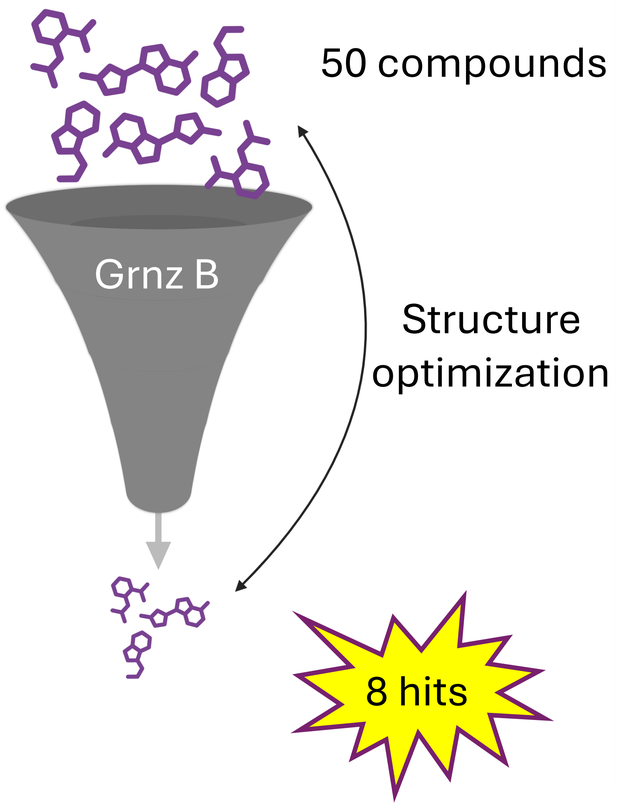
Aims & Objectives

1. Compound Library Synthesis

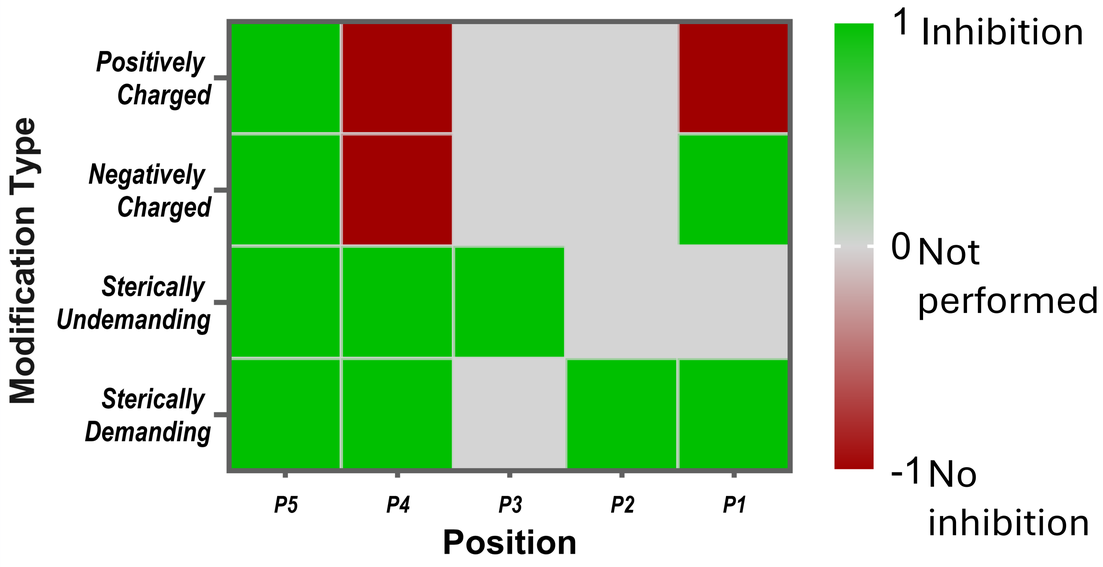


2. *In vitro* Biological Evaluation

A. Grnz B Screening

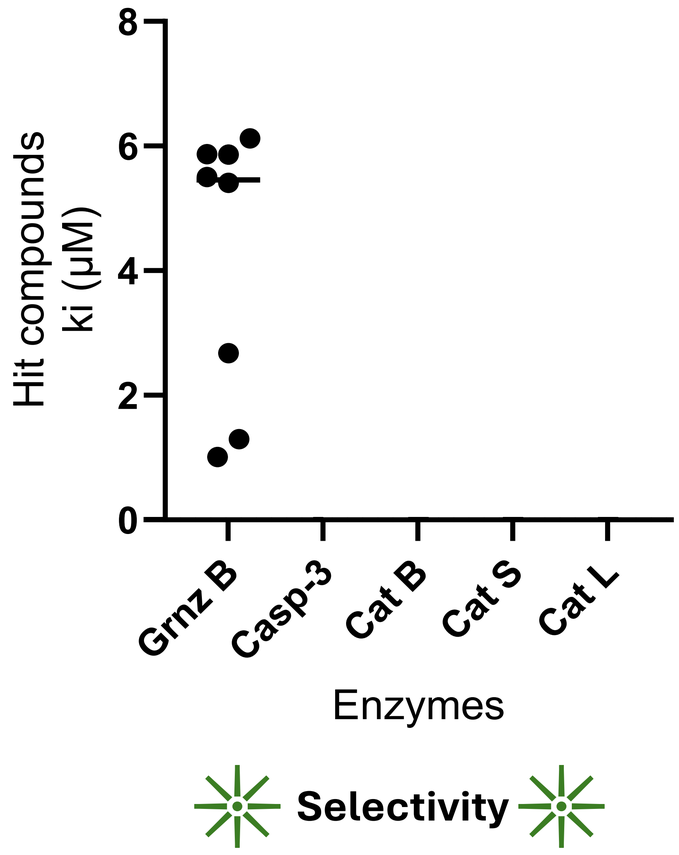


B. SAR Study

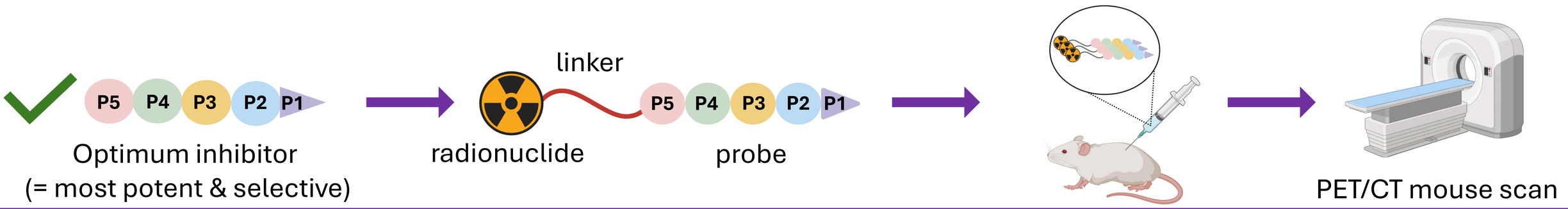


- ✓**P1** requires a **negatively** charged moiety
- ✓**P5** modifications are **well-tolerated**
- ✓**Low/no** tolerance in the **P2 – P4** modifications

C. Off-target Screening



3. *In vivo* Evaluation – Future Work



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Universiteit Antwerpen
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JOHANNES GUTENBERG UNIVERSITÄT MAINZ
Funded by the European Union

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

OncoProTools receives funding from the European Union's Horizon Europe Research and Innovation programme, under the Marie Skłodowska-Curie Actions (MSCA), Grant Agreement No 101073231