Granzyme B: a novel target for early cancer treatment response measurement via positron emission tomography (PET)

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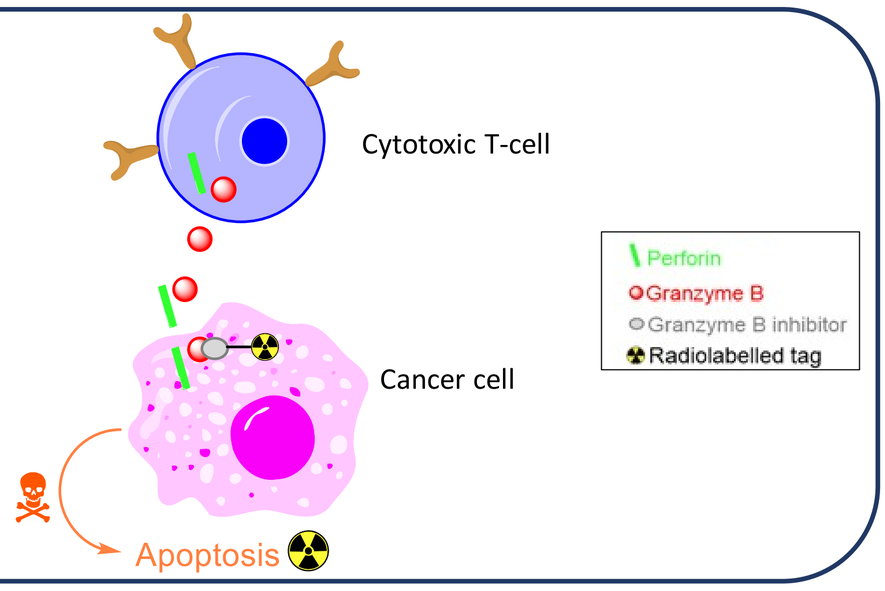
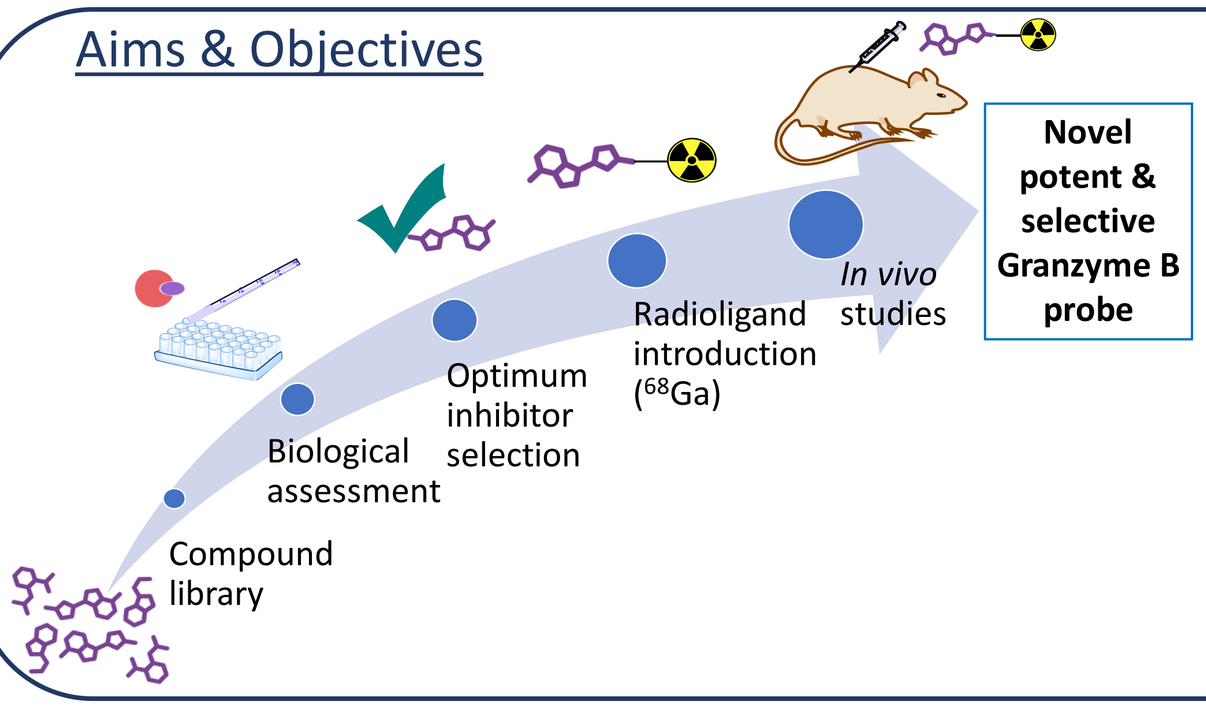
Introduction

- **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]
- Grnz B activates the **apoptotic pathway**, to cause DNA fragmentation and protein degradation that leads to **programmed cell death**.[1]
- Targeting Grnz B provides a **direct window to cancer treatment response.**
- In the framework **of CAR-T cell therapy**, intra-tumoral and extra-tumoral **GrnzB secretion** can be used as **a measure of therapeutic success and specificity**.[1]



Aims & Objectives



New potent and selective Grnz B probe with **reduced peptide & more drug – like** character.

Workflow

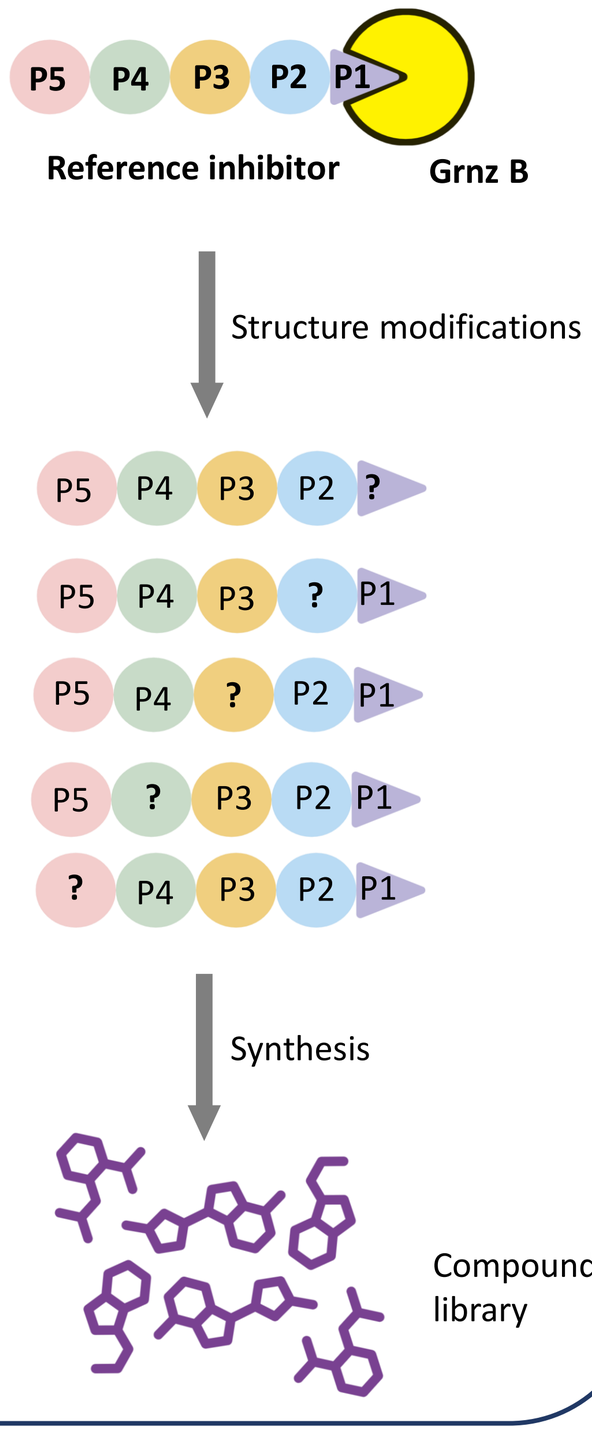
1. Compound library synthesis for **SAR- studies** to develop **a pharmacophore model.**

2. *In vitro* biological evaluation against **human Grnz B** and **A** and **caspases – 1, –3 and –8**.

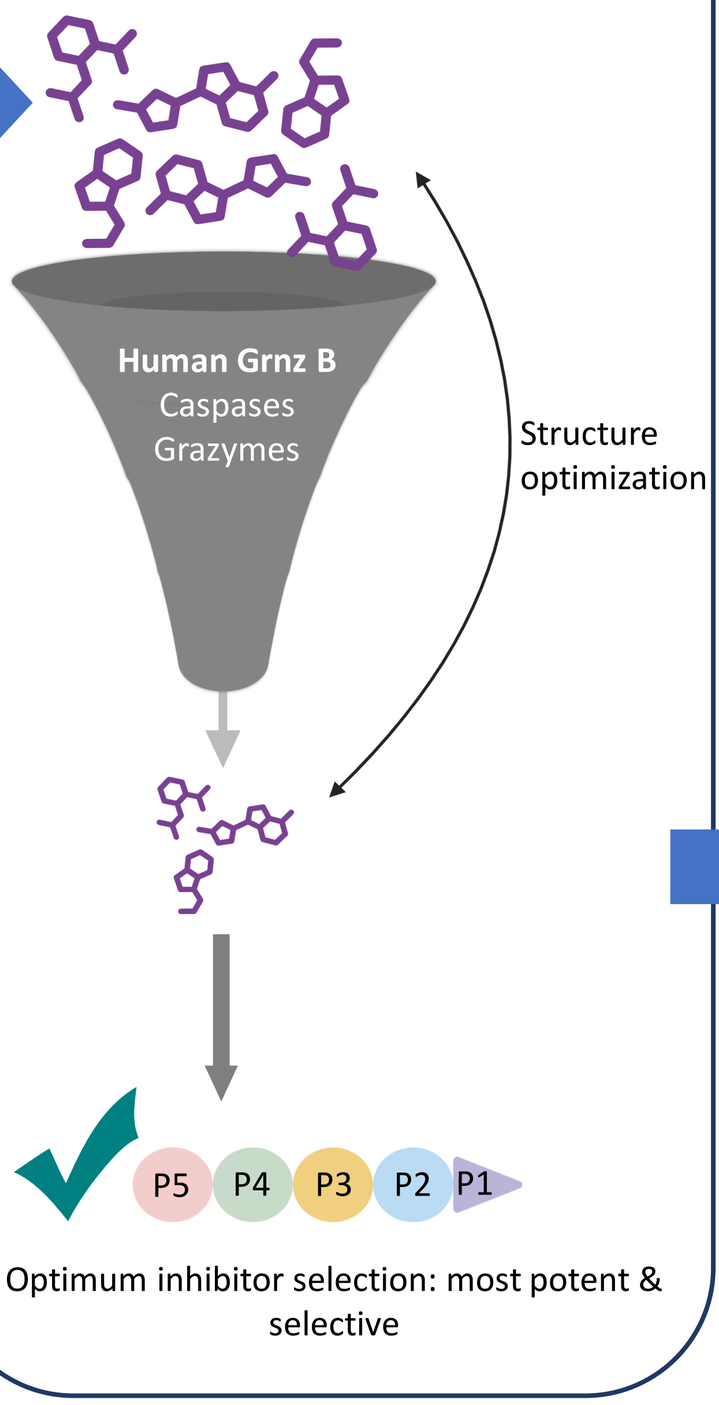
Optimum inhibitor *selection =>* ***probe***

3. *In vivo* probe assessment in tumor – bearing mice.

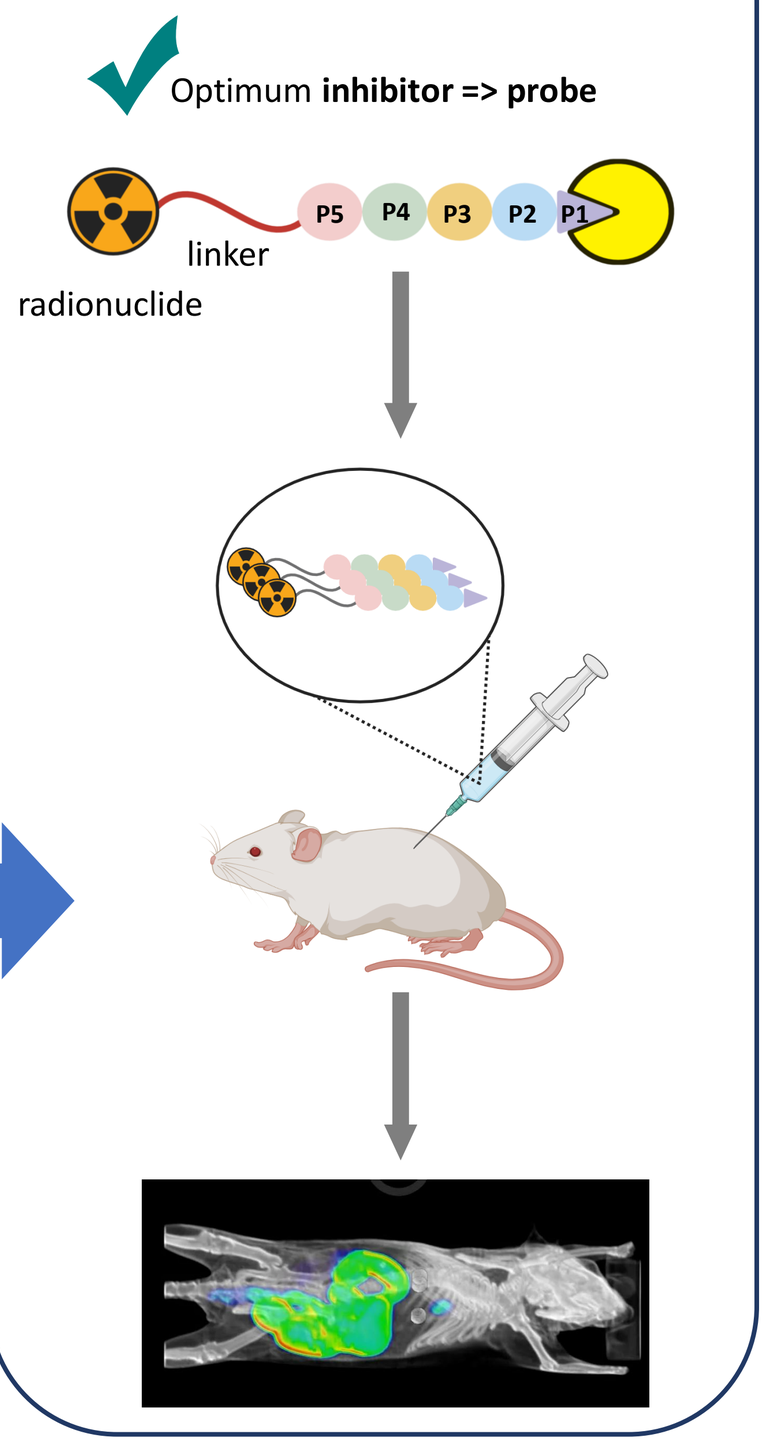
1. Compound Library Synthesis



2. *In vitro* Biological Evaluation



3. *In vivo* Evaluation



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

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