# **GRANZYME B: Design and discovery of novel probes** for early cancer treatment response imaging



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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 virus infected and tumor cells.<sup>1</sup>
- Grnz B activates the apoptotic pathway to cause DNA fragmentation and chromatin condensation that leads to programmed cell death.<sup>1,2</sup>
- 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.<sup>2</sup>



### AIMS AND OBJECTIVES

- Synthesis of novel Grnz B compound library to overcome selectivity against caspases and optimize potency.
- In vitro biological evaluation of the compound library against human and mouse Grnz B, A, H and caspases 3, –9 and –10.
- Selection of the **optimum** (most potent & selective) **inhibitor** to be converted into a **probe** (attachment of a linker with a tracer).
- In vivo & ex vivo probe assessment in tumor-bearing mice.

## METHOD







#### REFERENCES

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