Title

Heparanase inhibitors as anti-cancer medicines

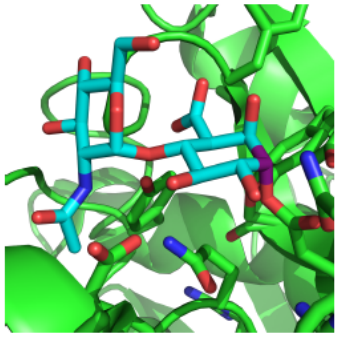
Authors

Gijs Ruijgrok, Vincent Lit, Yevhenii Radchenko, Valentina Borlandelli, Casper de Boer, Jeroen Codée, Hermen Overkleeft

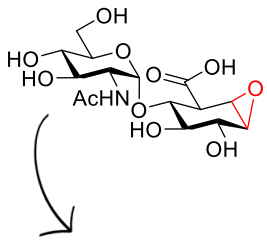
Poster presentation

Cancer's adaptability often leads to drug resistance and tumor progression despite early diagnosis, this presents a significant challenge in successful treatment. A key driver of this adaptability is the enzyme heparanase, it contributes to tumor growth, metastasis, and resistance to therapy, and is overexpressed in 90% of the known cancers.[1] We have developed and synthesized a proprietary library of covalent irreversible heparanase inhibitors based on the VL166 scaffold (Figure).
These inhibitors showed good inhibition of heparanase and excellent selectivity in blood platelet lysates, furthermore initial *in vivo* mouse models with VL166 showed a reduction in metastasis.[2]
Efforts are now ongoing to further develop this compound in a Spin-out company from Leiden University, Avigi Therapeutics.

Figure



Crystal structure with VL166



Library based on this scaffold

References

1. Jayatilleke, K.M., et al., Heparanase and the hallmarks of cancer. Journal of Translational Medicine, 2020. **18**: 453.
2. Boer de, C., et al., Mechanism-based inhibitors reduce cancer metastasis *in vivo*. Proceedings of the National Academy of Sciences of the United States of America, 2022. **119** (31).