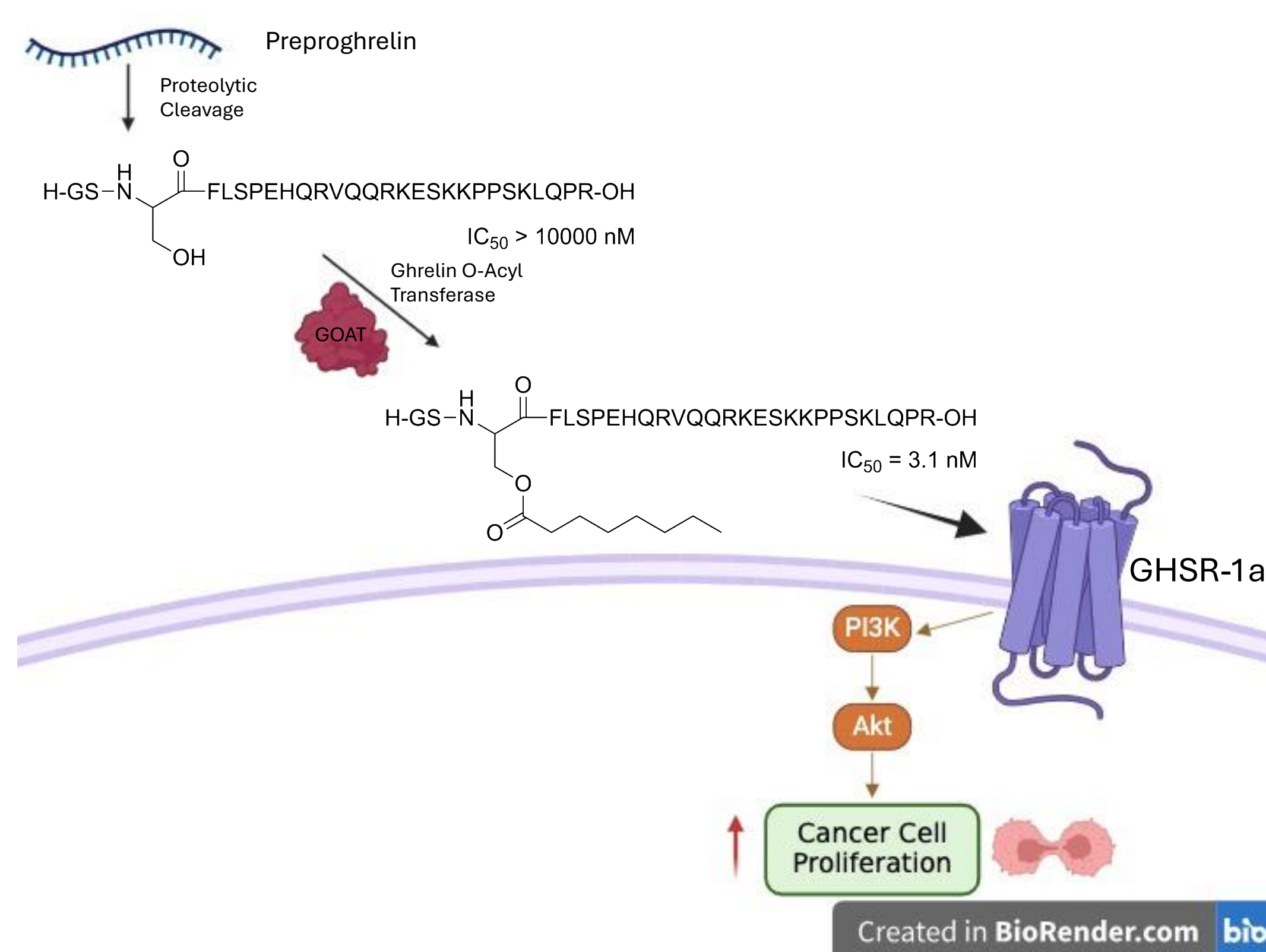


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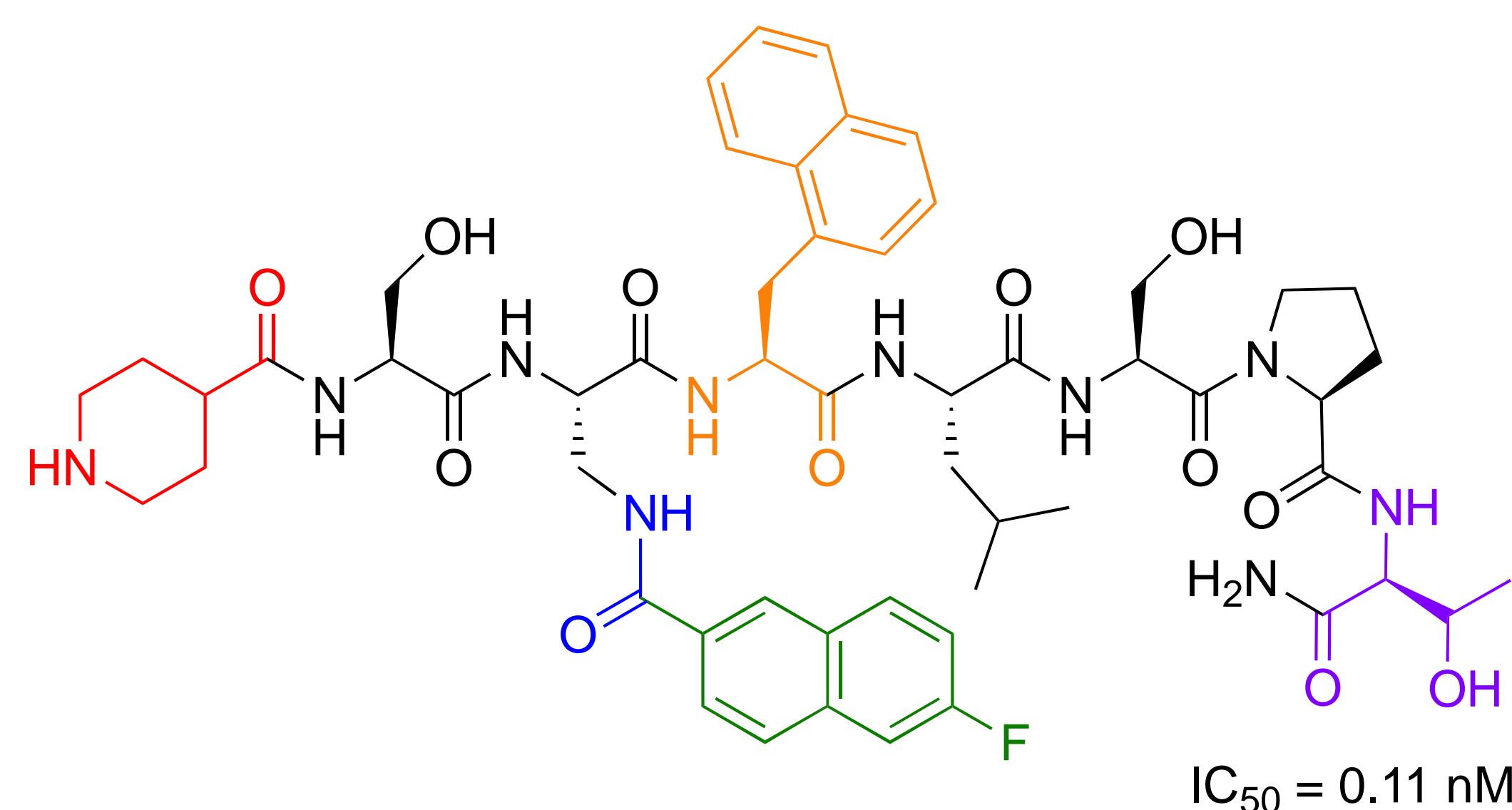
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The Ghrelin Receptor



Molecular imaging techniques, such as positron emission tomography (PET), have greatly benefitted the field of oncology with noninvasive methods for diagnosis and monitoring treatment progression. One approach is targeting cell surface receptors differentially expressed in disease states compared to healthy tissues, such as the ghrelin receptor, also known as the growth hormone secretagogue receptor. Many cellular processes are triggered upon binding to the endogenous ligand, ghrelin, regulating appetite, growth hormone release, and energy homeostasis. Activation of the receptor can also elicit several pathway including those that lead to increased cancer cell proliferation. The ghrelin receptor, expressed in the hypothalamus, pituitary gland, GI tract, myocardium, and pancreas, has been reported to be overexpressed in breast, prostate, and gastrointestinal endocrine tumours. Due to its role in many cancers, the ghrelin receptor is a potential target for cancer imaging and therapy.

Fluorine-Bearing Ghrelin(1-8) Analogue Discovery

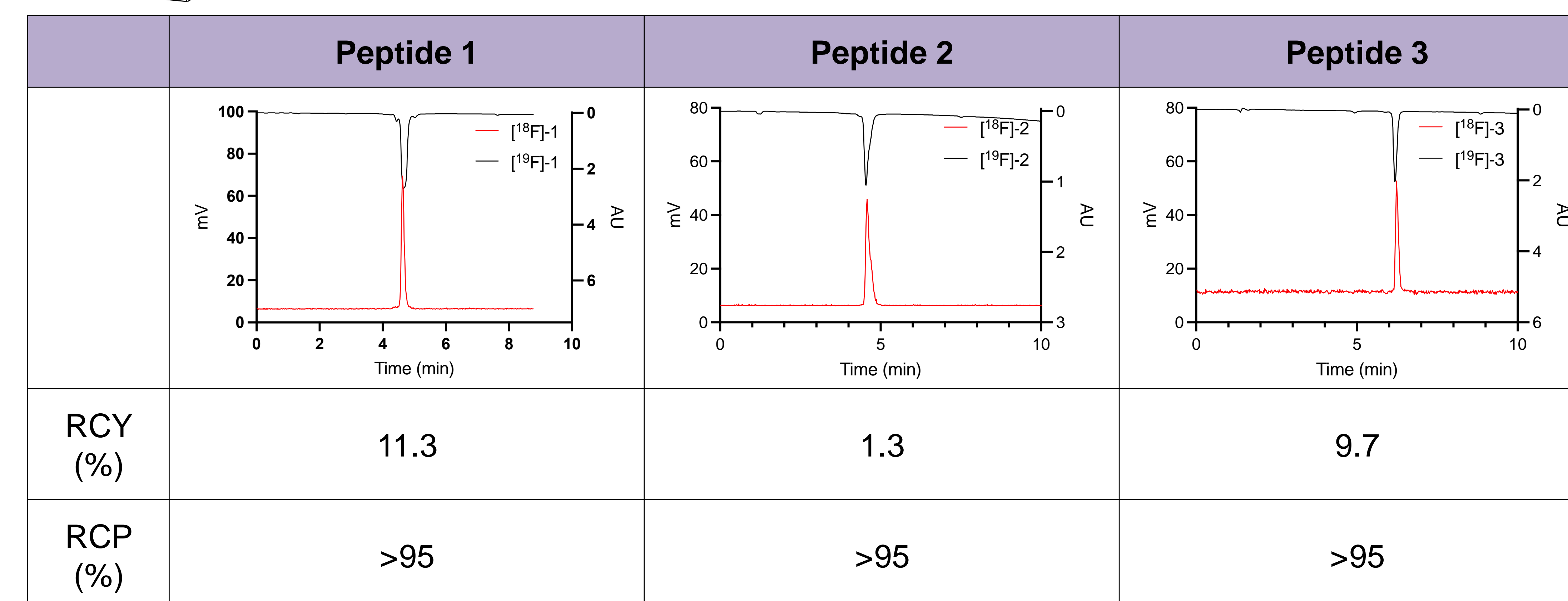
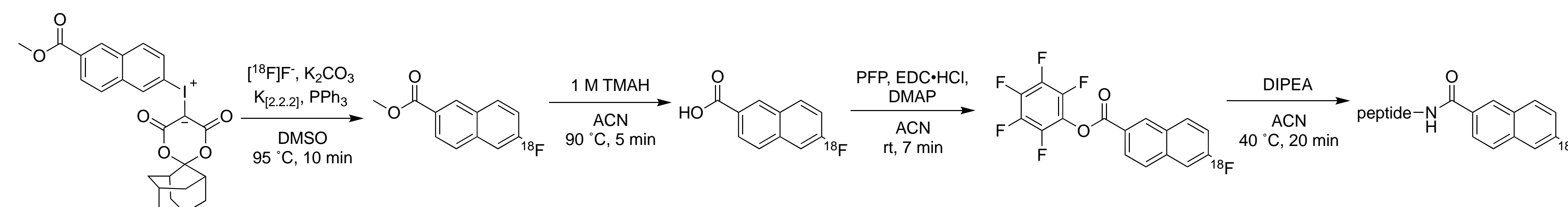


Extensive work has previously investigated truncated ghrelin, resulting in a peptide analogue with very high receptor affinity while also improving stability compared to natural ghrelin.¹ This study attached a fluorine-containing aromatic group at an amino acid side chain, providing structural access to a new PET imaging probe.

Improving Stability³

Peptide	Sequence	IC ₅₀ (nM)	Serum t _{1/2} (h)	Liver S9 t _{1/2} (h)
1	Inp-S-Dpr(6-FN)-1Nal-LSPT-NH ₂	0.11	4.7	1.08
2	Inp-S-Dpr(6-FN)-1Nal-LTPT-NH ₂	0.62	>24	1.25
3	Inp-S-Dpr(6-FN)-1Nal-L-S(N-Me)-PT-NH ₂	1.32	>24	>4

Peptide Radiosynthesis



Conclusion

A series of ghrelin(1-8) peptides were previously investigated to improve receptor affinity and stability. *In vivo* evaluation demonstrated high liver uptake and hepatobiliary excretion; thus, further modifications were done to improve proteolytic stability while retaining affinity. Three high affinity ghrelin(1-8) analogues have been successfully radiolabelled and are currently being investigated *in vivo* for their biodistribution in DU145 mouse xenografts as a prostate cancer model to access differences in pharmacokinetic profiles.

Acknowledgments

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Radiofluorination Method Optimization

