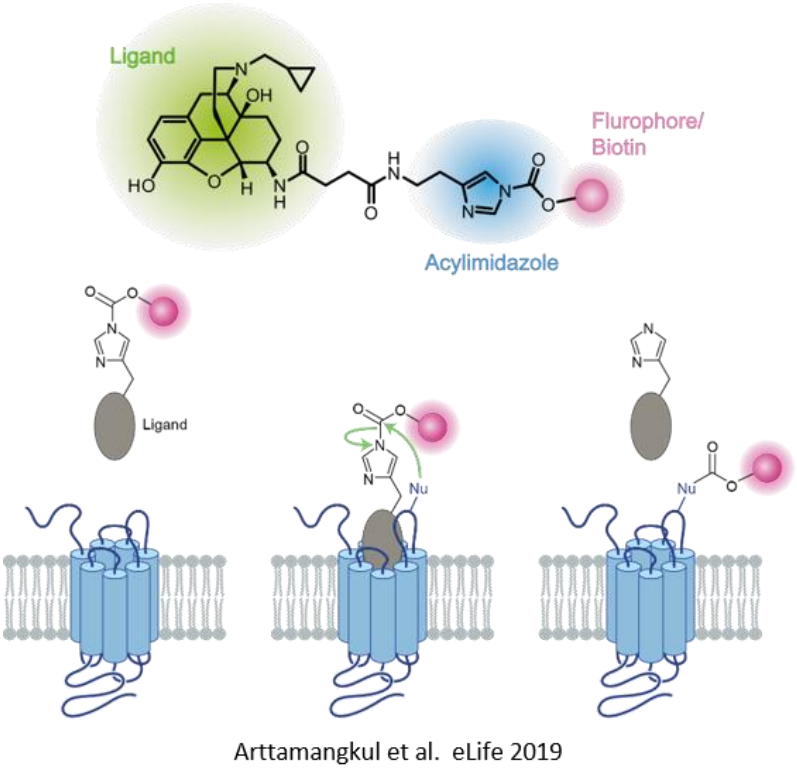
Naltrexamine acylimidazole for ligand-directed covalent labeling of endogenous receptors



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Ligand-directed covalent labeling is a method to endogenously label receptors using acylimidazole-modified ligands to guide and permanently attach small molecule reporters—such as fluorophores or biotin to receptors, which enables visualization and functional studies of the labeled receptor in live tissues or cell lines.

How does it work?

The acylimidazole-modified ligand is incubated with the cells or live tissue upon which the ligand binds to the receptor. The acylimidazole linker then reacts with a nucleophilic amino acid side-chain in proximity which results in the transfer of the small molecule reporter to the receptor. The ligand can then be washed out leaving a fully functional labeled receptor behind. This receptor can then be used in functional studies or the cells can be lysed and the receptor pulled out for proteomic analysis.

How can it work for you?

Step 1. Come to us with a known selective ligand for your receptor of choice and assays to determine binding and selectivity.
Optional: crystal structures or any other data about the binding site that can help us determine the optimal linker length and position.

Step 2. We will investigate if the ligand is commercially available and if so if we can do the modification using the commercially available ligand. If neither is true we will develop a synthesis from a commercially available precursor that will allow us to attach the acylimidazole linker.

Note: once we have synthesized the ligand with a part of the linker we will give you this precursor to test if the modified ligand still binds to its target and if the binding is still selective.

Step 3. Based on the available structural information we will determine a linker length and will attach the small molecule reporter of your choice.

Step 4. You can then test the compound for its labeling efficiency and if necessary we can modify the linker length to optimize labeling efficiency.