Medicinal Chemistry & Drug Discovery
Section 1.2.1 – Targets

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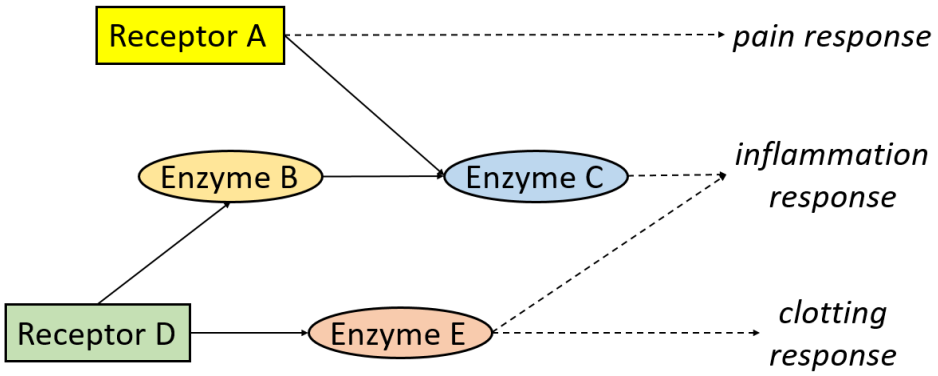
Learning goals

- prioritize different proteins in biological pathways as drug targets
- describe the role of an assay in the drug discovery process
- summarize the steps of identifying a lead through screening

Vocabulary

- drug target
- downstream
- druggable
- target-based drug discovery
- assay
- potency
- efficacy
- screening
- hit
- lead

The drug discovery process begins once an unmet medical need has been identified. The first step is research on the biological pathways associated with the disease. A hypothetic pathway for inflammation is shown below. The pathways are controlled by proteins – enzymes and receptors. The proteins produce and manage chemical messengers. Blocking or activating any of the proteins could influence inflammation. Each protein is a potential **drug target**. Proteins connected to just one response pathway are preferred, so Enzyme B and Enzyme C would be the most attractive targets. Targets closer to the response, or more **downstream**, are favored. The molecular biology team would study both Enzyme B and Enzyme C to see if either is more likely to be affected by a drug, i.e. **druggable**. Selecting a target is a key step in a **target-based drug discovery** program.



After target selection, the biology team will create a biochemical test that measures the activity of the target protein. The test, called an **assay**, allows quantification of a molecule's **potency**. Potency is related to the concentration of a drug required to cause an effect on a target. The assay also measures a molecule's **efficacy**, or the magnitude of the drug's effect.

The discovery team uses the assay to test the potency and efficacy of a large number of molecules against the selected target in a **screening** campaign. Over a million molecules may be tested. Screening campaigns are automated to increase speed and reproducibility. At the end of the campaign, the discovery team will have potency and efficacy data on all the screened molecules. The most promising compounds, called **hits**, may number in the hundreds or thousands. The very best hits will be promoted to **lead** status. A program may have multiple leads but normally just one will be the primary lead and advanced for further research. The other leads will be held in reserve as needed.