

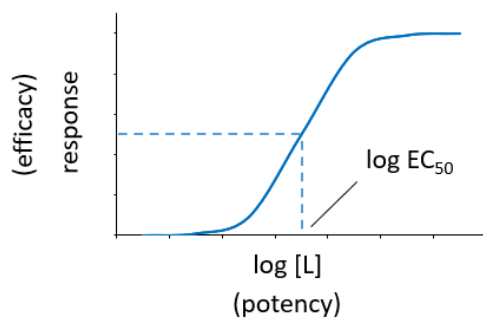
### Learning goals

- contrast potency and efficacy
- describe target validation

### Vocabulary

- efficacy
- target validation
- biomarker

The potency of an agonist can be read off of a response-vs-log[L] curve. The potency is on the x-axis as the  $\log[EC_{50}]$  value. The y-axis gives the response. The vertical change in the response on the y-axis is related to the **efficacy** of the molecule. Potency (the x-axis) and efficacy (the y-axis) are not equal. A molecule can have high efficacy but low potency. A molecule can have high potency but low efficacy. Ideally, a drug would have both high potency and high efficacy. The words efficacy and potency are often used interchangeably, but they do not have the same meaning.



Efficacy for an agonist means the molecule is turning on a receptor pathway. The goal of the molecule, however, is to treat a disease. Just because a molecule shows high efficacy and high potency in a binding assay does not mean the molecule will show efficacy against a disease in humans. The efficacy against a disease is not measured until Phase II clinical trials. This idea poses a real risk in drug discovery and is a major reason why so many molecules fail in Phase II clinical trials.

In order to minimize failure risks, drug companies continuously try to establish the value of a target for affecting a disease. This process is called **target validation** – making sure that binding the target with a molecule will yield therapeutic benefits in humans. Target validation may involve monitoring different molecules in the blood of animals during the animal studies. The monitored molecules are called **biomarkers**. Biomarkers are any molecule that can be measured. Biomarkers include anything from blood sugar or insulin to cholesterol or hormones. Researchers analyze biomarkers to establish that the target protein is having a positive, systemic effect on a disease. Biomarkers help connect the potency and efficacy of a molecule in a binding assay to its therapeutic value in patients.