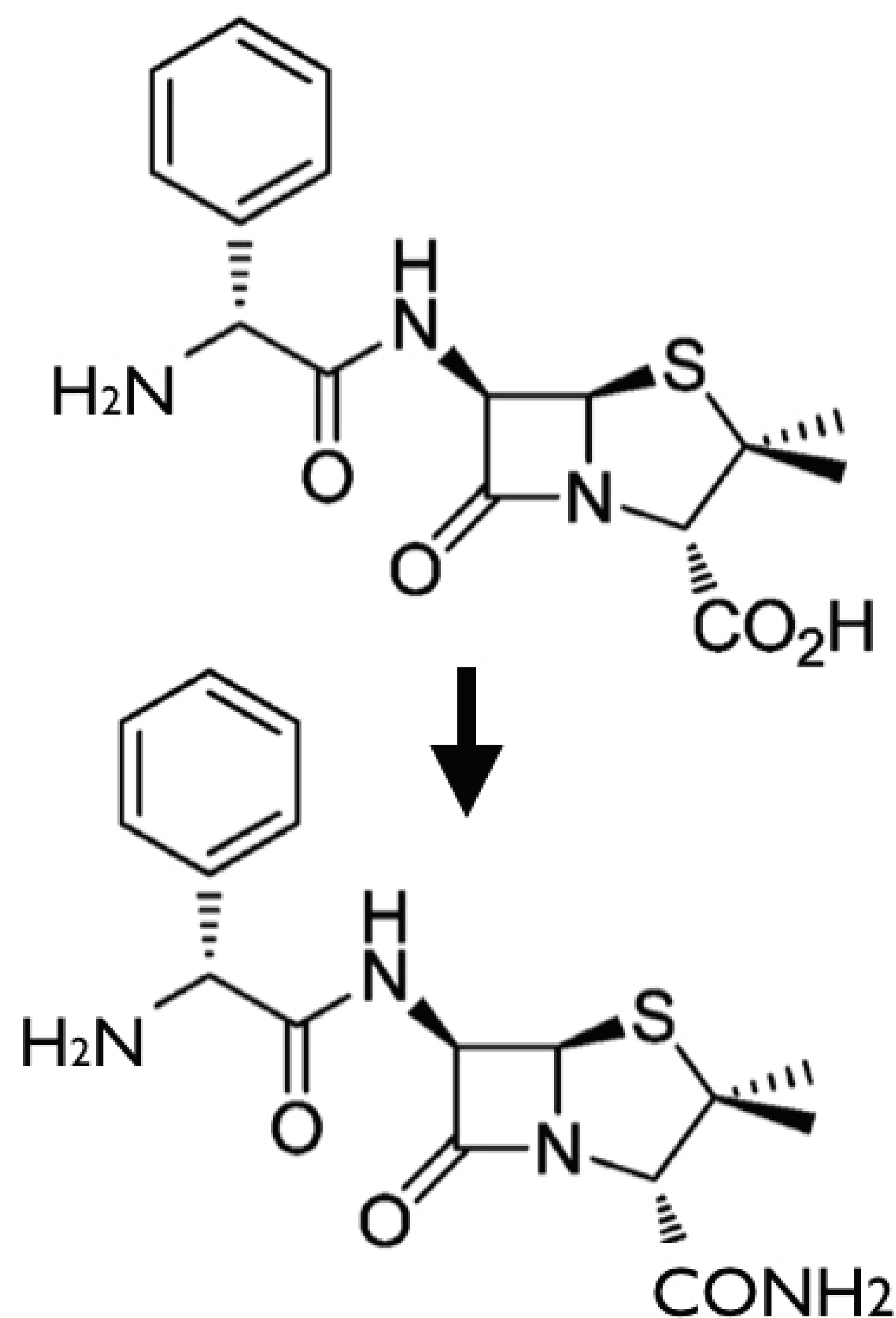

DEVELOPMENT OF BETA-LACTAMASE AS A SELF-LABELING PROTEIN TAG

Fluorescence microscopy is a major way that biologists examine cells and tissues. Self-labeling protein tags are a relatively new way of tagging proteins with fluorescent dyes. This method provides the advantages of genetically encoded tags (live labelling, and specificity) with the advantages of antibodies (bright fluorescence).

There are only 3 self-labeling proteins in wide use: Halo, SNAP and CLIP. A reasonable goal is to track ~5 proteins in a cell.

Since, we have found CLIP to be an ineffective tag, we only have two useful tags. We propose developing a new tag based on the protein beta-lactamase. Beta-lactamase is a small, monomeric enzyme with low-cost substrates available. It is possible to make the protein self-labeling via a single point mutation.

Unfortunately, the enzyme acts on charged substrates that cannot enter cells. We propose to develop cell-permeant substrates. The Jorgensen lab (Biology) will mutate the enzyme to accept uncharged substrates. The Hammond lab (Chemistry) will synthesize fluorescent substrates for the tag. The Stanfield lab (Human Genetics) will test the tag in vivo.

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