Center for Pharmaceutical Development (CPD)

Georgia Institute of Technology, Andy Bommarius, Director, 404.385.1334,
andreas.bommarius@chbe.gatech.edu

University of Kentucky, Eric Munson, 785.864.3319, eric.munson@uky.edu

Center websites: http://cpd.gatech.edu and cpd.uky.edu

Better/Cheaper Drugs: New Routes to Active Pharmaceutical Ingredients

Many active pharmaceutical ingredients, the part of a drug formulation responsible for its beneficial action, contain an amine group, similar to amino acids, the building blocks of life. Moreover, such amine groups have to be present as a single enantiomer and not a mixture, in other words the amine groups have to have a very specific orientation in space, or else the drug most often either is ineffective or even detrimental (recall the case of Thalidomide, where the presence of the wrong enantiomer causes birth defects).

Pure amines are difficult to synthesize, so difficult in fact that the Pharmaceutical Roundtable of the American Chemical Society Green Chemistry Institute listed the generation of such pure amines from easily accessible ketone precursors as the second highest priority for novel, aspirational reactions. A team of CPD researchers has developed a novel protein biocatalyst that achieves just such a transformation to amines from ketones. They started from a known protein biocatalyst and engineered it to accept ketones and to synthesize the desired amines in great stereochemical purity.

Being able to catalyze the conversion from ketone substrates to amine products is such an important addition to the toolbox that it stands to develop into a platform technology, applicable to the synthesis of a wide variety of targets in several therapeutic areas. Production of active pharmaceutical ingredients via biological routes stands to increase yields and shorten process routes via enhanced selectivity of key steps. One CPD sponsor intends to make use of this new ability for its own drug synthesis development efforts. The pharmaceutical company will receive the first batch of protein in 2012, less than one year after the ultimately successful protein template was first begun for development. The company indicated that it has several potential targets to which it will apply this new technology.

Economic Impact: This technology could impact the synthesis of drugs that contain chiral centers adjacent to nitrogen by providing more efficient methods for their manufacture. Not only is this process considerably more economical than existing processes that use the traditional wholly chemical routes, but they also leave substantially reduced environmental footprints. The impact on the manufacture of a single blockbuster drug is can be in excess of a billion dollars over the lifetime of such a drug. In a comparable case, Merck recently published an improved route to the active ingredient of Januvia® and Janumet®, a drug soon to reach blockbuster status; that route is said to be at least 25% cheaper than the current one. In addition, such biologically-inspired manufacturing with reduced environmental footprints are welcomed by most communities because processes to secure procure permits are greatly facilitated. In summary, more efficient manufacture of pharmaceuticals will help to drive down the cost of drugs to patients and help keep high-end pharma industry manufacturing jobs in the US. As a result, this innovation can be expected to have broad economic impact across the pharmaceutical and fine chemical industries.

For more information, contact Andreas Bommarius, 404.385.1334, andreas.bommarius@chbe.gatech.edu