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Optimizing Medicinal Chemistry With Microfluidics and Mass Spectroscopy

A standard procedure in drug research is to take a molecule that shows promising anticancer activity and create dozens, or even hundreds, of closely related molecules to determine if any of these chemically related relatives are safer or more effective than the original molecule. This molecular tinkering process, however, is time consuming and expensive. It can also be difficult to accomplish when the original molecule is in short supply, as is often the case with drug candidates obtained from plants or marine organisms.

Enter microfluidics, which has the potential to conduct chemistry on a much smaller scale and in parallel tracks that would speed the process of generating large numbers of molecular modifications. In a paper published in the *Journal of the American Chemical Society*, Rustem Ismagilov, Ph.D., and colleagues at the University of Chicago show just how microfluidics chemistry can be done using nanogram quantities of rare biologically active molecules.

Ismagilov and his colleagues constructed a microfluidics device that creates discrete droplets, or plugs, of fluid that function as nanoscale chemical reactors. Each plug, containing a few hundred nanograms of a starting molecule and separated from its neighboring plugs by an inert carrier fluid, flows through the channels of a microfluidics device. There, chemical reactants are added to the plugs as they pass through T-shaped junctions joining the channels to various chemical reservoirs. Eventually, the plugs are deposited individually on a sample plate for analysis using MALDI mass spectrometry.

This work is detailed in a paper titled, “Microgram-scale testing of reaction conditions in solution using nanoliter plugs in microfluidics with detection by MALDI-MS.” This paper was published online in advance of print publication. An abstract is available at the journal’s website. View abstract.