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# Rosetta Briegel Barton Lecture

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CHEMISTRY AND BIOCHEMISTRY DEPARTMENT, THE UNIVERSITY OF OKLAHOMA NORMAN, OK 73019-3051 (405) 325-4811

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We Are Pleased to Announce A Seminar  
Presented By

**Brian Shoichet**  
University of California, San Francisco

Friday, April 28, 2023  
4:15 pm  
NWC 1313

*Following the Rabbit into Chemical Space*

Structure-based drug-discovery often begins with screens of compound libraries, using molecular docking. Recently, these libraries have expanded from three million "in-stock" to over four billion diverse, stereogenic, and readily available molecules. These "tangible" molecules have not previously been synthesized, and do not exist until they are requested, and the only way to prioritize them for testing is computationally. In the last three years, campaigns against the dopamine, melatonin, and Sigma2 receptors have found novel chemotypes with high potencies directly out of the docking screen. Here, I will describe recent applications to the discovery of novel analgesics active against the  $\alpha$ 2a-adrenergic GPCR, and against the 5HT2a GPCR and the serotonin transporter to treat depression. The role of the large libraries in these applications, and whether the library merits still further expansion, will be considered.

Refreshments will be served