Profile of an Early-Career Researcher

Steven T. Staben, PhD

Associate Director and Senior Scientist
Genentech, Inc.
South San Francisco, California

Our theme for this issue involves the contributions of rational drug design to precision medicine. This month's profiled Early Career Investigator has spent a good portion of his first years in the pharmaceutical industry doing exactly this type of work.

Steve Staben, Ph.D. is currently an Associate Director and Senior Scientist in the Discovery Chemistry group at Genentech, in South San Francisco, California, USA. He joined Genentech in 2007 after completing his Ph.D. with Professor Dean Toste at the University of California, Berkeley. Part of Dean's first class of graduate students, Staben discovered and developed new organic- and transition-metal- catalyzed methodologies and contributed to the total synthesis of three natural products. While at UC Berkeley, he received several awards including the Gerald K. Branch Fellowship in 2004, the Klaus and Mary Saegebarth Fellowship in 2006, and the Roche Excellence in Chemistry Award in 2005. Prior to his graduate studies, he obtained his Bachelor's degree in chemistry in 2002 from Western Washington University, where he pursued undergraduate research with Professor James Vyvyan and was recognized as a University Outstanding Graduate.

Historically known for success in large molecule therapeutics, Genentech has more recently established expertise, commitment and significant success in small molecule research. Today, small molecules represent roughly half of Genentech's research pipeline and Steve leads a large chemistry team and interdisciplinary project teams in this space. As a medicinal chemist, Steve leverages an organic chemist's knowledge of physical properties, reactivity, molecular conformation, and interaction energies to design inhibitors of a variety of therapeutic targets.

Steve has spent a majority of his time at Genentech devoted to kinase inhibitor discovery for oncology and other indications – publishing work detailing the discovery of inhibitors of NF-κB inducing kinase (NIK), group-II p21-activated kinases (PAKs), protein kinase D1 (PKD1), and phosphoinositide-3-kinase (PI3K) inhibitors with variant isoform selectivity profiles. Within this work, he has demonstrated use of property- and structure-based design concepts to control inhibitor potency and selectivity as well as ADME properties. Most notably, Steve is a key contributor to a series of PI3K inhibitors including clinical molecules GDC-0032 (taselisib) and GDC0077. Steve led the interdisciplinary project team that discovered GDC-0077 – a highly PI3Kα-isoform selective inhibitor that promotes the selective loss of mutant-p110α over wild-type-p110α.

He has coauthored 25+ peer-reviewed publications and has over 20 published patent applications. He has been an invited speaker to give first disclosures of some of this work, including the 2017 AACR New Drugs on the Horizon Symposium, the 2016 and 2018 Gordon

Medchem Conference and the Spring 2018 ACS Medi Young Investigator Symposium. Steve maintains basic research interests in chemical biology, unique therapeutic modalities and novel strategies for inhibitor design and continues to publish new methodologies in these areas. We look forward to additional discoveries emerging from the lab of this outstanding young drug hunter!