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All roads to successful drug discovery lead through cell-based assays (and why shouldn't they?)

Abstract

There are a number of daunting challenges to be faced in modern day drug development. These include intense competition from amongst domestic and foreign pharmaceutical and biotechnology interests with respect to intellectual property, "orphan" drug targets with sparsely-associated literature annotation, and a high public and FDA demand for novel specific drugs with high efficacy and low toxicity profiles. Increasingly, cell-based assays have consistently provided value-adding information to a number of core aspects in the quest for new medicinals by (1) enabling cellular phenotypical characterization of inhibitory RNA knockdown of candidate proteins from all classes of drug targets (2) allowing the investigation of these targets in the correct cellular context, with pathway interactions and signaling responses intact (3) discriminating between desirable on-target and undesirable off-target functional effects, especially in cases where the latter can obscure the former (4) providing metrics for measuring the new physiological steady state which is established in the face of prolonged drug exposure (5) supporting early de-risking strategies using cellular estimates of genotoxicity and cytotoxicity as surrogates for eventual and inevitable in vivo data.

Resume

Dr. Ralph J. Garippa was appointed the Head of Cell-Based High Throughput Screening (HTS) and Microscopic Imaging-based High Content Screening (HCS) at Hoffmann-La Roche's Nutley facility, effective March 1999. As such, his group is responsible for the assay development, HTS, and automation support required for the therapeutic areas of Oncology, Inflammation, and the Metabolic Diseases areas of diabetes and obesity. He has previously been a Roche site manager for the Perkin Elmer / Evotec-Zeiss Ultra High Throughput Screening platform and is also currently a member of the Scientific Advisory board for the MLSCN Roadmap Project at the NIH. Presently, he is leading a cross-functional team towards the integration of automated high content screening (HCS) imaging tools into the hit-to-lead and lead optimization strategies for several in-house projects. From 1982 to 1998, he served in various positions at Roche, including Project Manager in Metabolic Diseases (1994-1998) and Laboratory Leader in Bronchopulmonary Pharmacology (1986-1992). Dr. Garippa holds a Ph.D. in Pharmacology from Columbia University in New York City (where he studied with Drs. Fred Maxfield and Tim McGraw) and a B.A. degree in Biology from Fairleigh Dickinson University in New Jersey (where he studied with Dr Gervasia Schreckenbergl).