

Dr. G. Jagadeesh



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Gowraganahalli Jagadeesh received his undergraduate degree in pharmacy from the Government College of Pharmacy affiliated then to Bangalore University. He completed his master and doctoral degrees at the All-India Institute of Medical Sciences, New Delhi, and Banaras Hindu University, Varanasi, respectively. He also worked/studied for a brief time at Hamdard College of Pharmacy and Institute of History of Medicine and Medical Research, New Delhi, and Post-Graduate Institute of Medical Education and Research, Chandigarh. In 1975, he joined the faculty at the Department of Pharmaceutics, BHU (and completed Ph.D. as a teacher candidate) and rose to become Reader in Pharmacology. He was a Canadian Heart Foundation Fellow at the University of Saskatchewan (Department of physiology, College of Medicine), Canada, from 1982 to 1984. He returned to India in 1985 and moved to the United States in 1986 to join as a Staff Scientist (NIH research fellow) at Northeastern University College of Pharmacy, Boston. Besides doing research, he also taught undergraduate and graduate classes (1986-1990). Dr. Jagadeesh began his affiliation with the US Food and Drug Administration at Silver Spring, Maryland, in 1990 where he is presently an Expert Pharmacologist in the Division of Cardiovascular and Renal Products, Office of New Drugs, Center for Drug Evaluation & Research. At the FDA, he reviews and evaluates the results of preclinical pharmacological, ADME, and toxicological studies submitted in support of INDs, NDAs, amendments, supplements and reports to new drug applications, to assess the safety of the drug based on toxicity experiments conducted by the applicant. Reviews the animal data included in proposed labeling to determine if the animal studies support the manufacturers' claims for safety. His skill lies in the areas of drugs targeting the renin angiotensin aldosterone system and calcium channels.

Besides working for full time at the FDA, he worked (1991 to 2004) as an Adjunct Scientist at Endocrinology and Reproduction Research Branch, National Institute of Child Health and Human Development, National Institutes of Health, Bethesda, Maryland. His expertise is in cardiovascular and autonomic receptor pharmacology, G Protein-coupled receptors and Signal Transduction. His research has focused on the structure-functional characterization of adrenergic, muscarinic and angiotensin receptors in vascular and cardiac muscles and COS-7 cells, and has authored or co-authored over 30 scientific papers that address these topics. Besides, he has authored several review articles, contributed chapters and edited books. He is a peer reviewer for several journals, grant proposals and thesis examiner for many universities. In addition to the above activities, Dr. Jagadeesh serves on several scientific committees, editorial boards, and in professional organizations.

Drugs and Drug Targets

The main focus of drug discovery has been on protein drug targets that play a key role in disease pathogenesis. Determination of the optimal molecular targets for drug intervention provides the basis for the discovery of new medicine. The advent of genomic science has advanced our knowledge in the development of new pharmaceuticals as we have increased our understanding of how genes are linked to diseases and code for proteins. It is estimated that approximately 10% of all genes (2500 to 3000) are linked to diseases. Targeting individual genes in the drugome is not an ideal task, because the functional product of each gene is under multiple regulatory controls. Thus, targeting a proteome is ideal because druggability is an inherent property of the protein. Nearly half of the disease-associated proteins are not druggable as they lack hydrophobic binding sites for a potentially orally delivered, membrane-permeable drug molecule. This restricts the number of potential drug targets, which is estimated to be 2-5% of the genome (600-1500 novel drug targets).

Over the past thirty years (1982 to 2010) of drug target innovation, on average, ~18 new drugs targeting human proteins have been approved by the FDA every year, of which ~4 are first-in-class that act on novel target structures that are encoded by the human genome, and the remaining are follower drugs (*Rask-Andersen et al. Nature Rev Drug Discov 10:579, 2011*). According to the authors, this translates to 435 drug targets. Enzymes are the largest target (47%) followed by receptors (GPCR accounts for 30%, the second largest), transporters (voltage-gated calcium channels, the largest) and others. The most common action of the approved drugs is antihypertensive followed by anticancer, anti-inflammatory, hypnotic and

sedative, anti-allergic, anticonvulsant, anti-arrhythmic, antipsychotic, antidepressant and analgesic. Most drugs target only a few proteins but some have targets as high as 19 (e.g., bromazepam). The average number of target proteins per drug is 1.8 (*Yildirim et al. Nature Biotech 25:1119, 2007*) surpassing the number of single target drugs, and thus, are called target multipliers (polypharmacology). Multi-target drugs are useful in cases where specific disease-associated proteins are not druggable. Interactions between proteins (interactome), drugs (drug network), drug and target (drug-target network) and disease and disease gene (diseasome) are studied in the field of network biology.

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