



Ramesh Shivdasani, M.D. Ph.D.

Dr. Ramesh Shivdasani's work focuses on understanding the genetics of carcinoid tumors. By defining the genetic mutations that drive the development of carcinoid, Dr. Shivdasani hopes to pave the way for new targeted therapies for carcinoid tumors.

Dr. Shivdasani is using a variety of genetic approaches to mine the carcinoid tumor bank that has been created at the Dana-Farber Cancer Institute, the largest collection of carcinoid tumors. His first approach involves using single nucleotide polymorphism (SNP) arrays to analyze the genome of carcinoid tumors. This technique identifies genes that have increased or decreased copy numbers due to mutation in carcinoid tumors, compared with normal tissue. SNP array analysis has been conducted on both primary tumors and metastases from the same patient, to help identify genetic alterations that may be involved in metastatic tumor spread. By identifying genes that are amplified in copy number or deleted in tumors, Dr. Shivdasani can delineate what genetic events might be important in tumor formation and may serve as targets for potential therapies.

Dr. Shivdasani's second approach involves using the OncoMap technique to analyze carcinoid tumors for gene mutations. This technique allows high efficiency sequencing of genes that are commonly present in a wide range of tumors. Dr. Shivdasani's lab has performed this analysis on over 100 carcinoid tumors. From preliminary results, his group has already identified a mutation present in a small fraction of intestinal carcinoid tumors, which suggests that a specific gene pathway could be important in carcinoid development. Drugs that block this gene pathway may find a role in treating selected patients with carcinoid tumors, and Dr. Shivdasani's team is exploring this possibility.

Finally, Dr. Shivdasani is using mouse genetics to identify the specific cell of origin of carcinoid tumors. By tagging specific lineages of enteroendocrine cells in the developing gut, Dr. Shivdasani hopes to learn more about how carcinoid tumors arise. A better understanding of the origins of carcinoid could offer new strategies for tumor prevention or treatment.

Recent Publications:

Kim BM, Mao J, Taketo MM, Shivdasani RA. Phases of canonical Wnt signaling during the development of mouse intestinal epithelium. *Gastroenterology* 2007 133:529-538.

Choi MY, Romer AI, Hu M, Lepourcelet M, Mechoor A, Yesilaltay A, Krieger M, Gray PA, Shivdasani RA. A dynamic expression survey identifies transcription factors relevant in mouse digestive tract development. *Development* 2006 133:4119-4129.