

Scientists illuminate how microRNAs drive tumor progression

September 17 2009

(PhysOrg.com) -- UCSF researchers have identified collections of tiny molecules known as microRNAs that affect distinct processes critical for the progression of cancer. The findings, they say, expand researchers' understanding of the important regulatory function of microRNAs in tumor biology and point to new directions for future study and potential treatments.

The researchers refer to these microRNA collections as signatures, and their study results are reported in the September 15 issue of "[Genes & Development](#)." The study, available online at <http://genesdev.cshlp.org/>, was led by the laboratory of Douglas Hanahan, PhD, an American Cancer Society Research Professor in the Department of Biochemistry and Biophysics at UCSF.

Approximately five percent of all known human genes encode, or produce, microRNAs, yet scientists are only now - nearly a decade after their discovery -- beginning to unlock the mystery of their functions.

MicroRNAs are snippets of single-stranded RNAs that prevent a gene's code from being translated from messenger RNA into proteins, which are essential for cell growth and development. Produced in the nucleus and released into the cytoplasm, they home in on messenger RNAs that possess a stretch that is complementary to their genetic sequence. When they locate them, they latch on, preventing the messenger RNA from being processed by the protein-making machines known as ribosomes. As such, microRNAs are able to ratchet down a cell's production of a

given protein.

Over the last several years, several groups have identified hundreds of microRNAs that are deregulated between normal tissue and tumors, however researchers only understand what a handful of these powerful regulators are doing to drive tumor formation.

"Virtually all cancers acquire approximately six distinct capabilities en route to tumor formation," said lead author Peter Olson, PhD, a postdoctoral fellow in the Diabetes Center and Helen Diller Family Comprehensive Cancer Center at UCSF. "When a [cancer](#) researcher observes a gene or microRNA go awry, it can be challenging to understand how that microRNA impacts tumorigenesis."

To home in on the question, the authors turned to a mouse model of pancreatic neuroendocrine tumors in which lesions go through discrete stages before culminating in invasive and metastatic carcinomas. In the three-year microRNA study, they found that cells in the mouse model developed and functioned normally but started to replicate uncontrollably at five weeks. Several weeks later, some pancreatic islets had become angiogenic (forming new blood vessels) - a step in the journey from a dormant state to a malignant state -- though had not yet formed a tumor. By 10 weeks, a subset of angiogenic lesions had progressed to the tumor stage, and by week 16, a small percentage of mice had developed liver metastasis.

"This represents the spectrum of stages that we think are important for all tumors, including human disease," said Olson.

By measuring the expression level of all known microRNA in pre-tumor stages, tumors and metastases, the authors were able to associate deregulated microRNAs with processes such as hyperproliferation, angiogenesis and metastasis.

Focusing on the metastatic signature, researchers found -- in one of the most striking observations of the project -- that tumors bore a startlingly divergent [microRNA](#) expression pattern compared to primary tumors. Moreover, a subset of primary tumors showed more similarity to metastases than to other primary tumors.

"If you can identify tumors that have an increased propensity to metastasize, then it would have a very important clinical application," said Olson. "A lively debate in metastatic research has centered around whether primary tumor cells must suffer an additional mutation that endows that cell with a metastatic capability, or whether certain mutational combinations that are responsible for primary [tumor formation](#) also significantly increase the propensity of that cell to metastasize. These data provide evidence for the latter."

Source: University of California - San Francisco

Citation: Scientists illuminate how microRNAs drive tumor progression (2009, September 17) retrieved 27 April 2024 from <https://medicalxpress.com/news/2009-09-scientists-illuminate-micrornas-tumor.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--