# GRANT SNAPSHOT

**2003 Pancreatic Cancer Action Network – AACR Career Development Award**

<table>
<thead>
<tr>
<th><strong>Grantee:</strong></th>
<th>David Tuveson, MD, PhD</th>
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<tr>
<td><strong>Institution:</strong></td>
<td>Cambridge Research Institute, Cancer Research UK</td>
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<td><strong>Project Title:</strong></td>
<td><em>Tumor Suppressor Gene Loss of Heterozygosity for the Generation of a Murine Model of Ductal Pancreatic Cancer</em></td>
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<td><strong>Award Period:</strong></td>
<td>July 1, 2003 – June 30, 2005</td>
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<tr>
<td><strong>Amount:</strong></td>
<td>$100,000</td>
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### Biographical Highlights

Dr. Tuveson is Senior Group Leader at the Cancer Research UK Cambridge Research Institute, which is linked to Cambridge University and is the latest cancer research initiative in the UK. Dr. Tuveson’s lab investigates the essential components of malignant transformation of pancreatic cells and translates this knowledge into effective tumor detection and treatment strategies. Dr. Tuveson earned his MD and PhD from The Johns Hopkins University and completed a medical residency at Brigham and Women's Hospital and a medical oncology fellowship at Dana-Farber/Partners Cancer Care. From 2002 – 2006, he was Assistant Professor of Medicine at University of Pennsylvania. In 2006, he moved his laboratory to the Cambridge Research Institute to develop a large therapeutics and genetics program in pancreatic cancer. Dr. Tuveson is a member of the Pancreatic Cancer Action Network Scientific Advisory Board.

### Project Description

Genes involved in promoting cell growth are called oncogenes, while genes that stop cell growth are called tumor suppressor genes. Mutations that cause increased activity of oncogenes and decreased activity in tumor suppressor genes are often found in cancer cells and precancerous cells. Mutations of a specific oncogene, Kras, have been identified in early cancers, and even prior to the formation of a tumor. Thus, Kras mutations may play a role in the start of pancreatic cancer, with mutations in specific tumor suppressor genes occurring later in the development of the tumor. Dr. Tuveson’s laboratory has developed an animal model of pancreatic cancer by generating mutant mice with Kras mutations. The mice have precancerous lesions similar to those found in humans. The goal of the funded project is to develop a model to evaluate the mice that develop both this precancerous lesion and the mutations of the tumor-suppressor genes. Once this model has been developed, tumor formation can be better assessed. In addition, this may allow for new detection and treatment strategies.

### Results/Outcomes

The mouse model that resulted from this project has been freely disseminated to other academic groups and has become the benchmark resource for a variety of laboratories throughout the world. The co-developer of the model, Sunil Hingorani, has started his own lab at the Fred...
Hutchison Cancer Center in Seattle, where he is pursuing research on the biology, detection and therapy of pancreatic cancer. Nabeel Bardeesy and Sam Hanash at Massachusetts General in Boston have modified the early model and used their product to identify new biomarkers for pancreatic cancer. In his lab at Cambridge UK, Dr. Tuveson is working to understand the failure of today’s therapeutic approaches in pancreatic cancer and to develop effective strategies to overcome these failures.

Lessons Learned
Dr. Tuveson attributes the ultimate success of the project largely to collaborations that were established with groups who were already involved in pancreatic cancer or developmental biology research. He recommends newcomers to the field to contact and speak to potential collaborators early in their careers and to attend national meetings.

Next Steps
Dr. Tuveson was able to parlay early successes into a large effort and, ultimately, moved his laboratory to a foreign country in efforts to make more progress. He is exploring a specific objective: whether an academically-based effort that is robust and well supported can make relevant breakthroughs in the therapy of pancreatic cancer. Ultimately, active drugs are needed for pancreatic cancer patients, and none have yet been identified.

Follow-Up Funding
Dr. Tuveson reports that the Pancreatic Cancer Action Network – AACR Grant “…allowed me to develop this early mouse model to the point where we published an important paper and secured an NIH R01 grant. Achieving an R01 grant is the penultimate rite of passage in academic biomedicine and (the Pancreatic Cancer Action Network) played an important role in this process.”

Publications Related to Funded Project


