[Sci Transl Med.](" \o "Science translational medicine." \t "blank) 2011 Jul 20;3(92):92ra66. doi: 10.1126/scitranslmed.3002543.

# Recurrent GNAS mutations define an unexpected pathway for pancreatic cyst development.

[Wu J](/pubmed?term=Wu%20J%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Matthaei H](/pubmed?term=Matthaei%20H%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Maitra A](/pubmed?term=Maitra%20A%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Dal Molin M](/pubmed?term=Dal%20Molin%20M%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Wood LD](/pubmed?term=Wood%20LD%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Eshleman JR](/pubmed?term=Eshleman%20JR%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Goggins M](/pubmed?term=Goggins%20M%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Canto MI](/pubmed?term=Canto%20MI%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Schulick RD](/pubmed?term=Schulick%20RD%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Edil BH](/pubmed?term=Edil%20BH%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Wolfgang CL](/pubmed?term=Wolfgang%20CL%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Klein AP](/pubmed?term=Klein%20AP%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Diaz LA Jr](/pubmed?term=Diaz%20LA%20Jr%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Allen PJ](/pubmed?term=Allen%20PJ%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Schmidt CM](/pubmed?term=Schmidt%20CM%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Kinzler KW](/pubmed?term=Kinzler%20KW%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Papadopoulos N](/pubmed?term=Papadopoulos%20N%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Hruban RH](/pubmed?term=Hruban%20RH%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank), [Vogelstein B](/pubmed?term=Vogelstein%20B%5BAuthor%5D&cauthor=true&cauthor_uid=21775669" \t "blank).

### Source

Ludwig Center for Cancer Genetics and Howard Hughes Medical Institutions, Johns Hopkins Kimmel Cancer Center, Baltimore, MD 21231, USA.

### Abstract

More than 2% of the adult U.S. population harbors a pancreatic cyst. These often pose a difficult management problem because conventional criteria cannot always distinguish cysts with malignant potential from those that are innocuous. One of the most common cystic neoplasms of the pancreas, and a bona fide precursor to invasive adenocarcinoma, is called intraductal papillary mucinous neoplasm (IPMN). To help reveal the pathogenesis of these lesions, we purified the DNA from IPMN cyst fluids from 19 patients and searched for mutations in 169 genes commonly altered in human cancers. In addition to the expected KRAS mutations, we identified recurrent mutations at codon 201 of GNAS. A larger number (113) of additional IPMNs were then analyzed to determine the prevalence of KRAS and GNAS mutations. In total, we found that GNAS mutations were present in 66% of IPMNs and that either KRAS or GNAS mutations could be identified in 96%. In eight cases, we could investigate invasive adenocarcinomas that developed in association with IPMNs containing GNAS mutations. In seven of these eight cases, the GNAS mutations present in the IPMNs were also found in the invasive lesion. GNAS mutations were not found in other types of cystic neoplasms of the pancreas or in invasive adenocarcinomas not associated with IPMNs. In addition to defining a new pathway for pancreatic neoplasia, these data suggest that GNAS mutations can inform the diagnosis and management of patients with cystic pancreatic lesions.

Dr. med. Hanno Matthaei  
Klinik und Poliklinik für Allgemein-, Viszeral-,  
Thorax- und Gefäßchirurgie  
Universitätsklinikum Bonn  
Sigmund-Freud-Str. 25, 53105 Bonn, Germany  
Telefon: 0228-287-15109