

'The Mentor's Quality Determines the Probability of Success of the Young Researcher'

An Interview with Prof. Makoto Otsuki

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Abstract

In this interview, Professor Makoto Otsuki points out the importance of mentorship during young researchers' development. Dr. Otsuki, a Professor and Chair of the Third Department of Internal Medicine at the University of Occupational and Environmental Health, has contributed significantly to the field of pancreatic physiology. In addition, his epidemiological research has been fundamental for understanding the pathogenesis of pancreatitis and establishment of the guidelines for its diagnosis and improvement of case fatality.

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Prof. Makoto Otsuki

M.E.F.-Z.: What initiated you to work in pancreas research in the first place?

M.O.: During my postgraduate course, I was engaged in research about the hypothalamus-pituitary-thyroid axis, in particular TSH-releasing hormone (TRH). I wrote and published a TRH test in patients with Cushing syndrome and in those treated with glucocorticoids [Influence of glucocorticoids on TRF-induced TSH response in man. *J Clin Endocrinol Metab* 1973;36:95–102]. However, when I completed the postgraduate course, the department in which I worked elected Professor Baba as the new chairman. Professor Baba specialized in diabetes mellitus and asked me to stop research in the endocrinol-

ogy field and instead concentrate on the study of amylase. Probably this was the start of my interest in the exocrine pancreas. I did my work with Professor Baba for more than 15 years as an assistant professor. Endocrine dysfunction of the pancreas causes diabetes mellitus. However, the pancreas does not only have endocrine glands (islets) that secrete hormones such as insulin and glucagon but also exocrine glands that secrete digestive enzymes that are delivered into the duodenum. Subsequently, I started my research investigating the relationship be-

tween exocrine and endocrine functions of the pancreas. However, I had no mentors but started this research by myself through trial and error. I visited several institutions to learn various techniques necessary to conduct pancreatic research and to discuss unsolved problems.

I learned how to prepare isolated perfused rat pancreas from Professor Kanno at the Department of Physiology, Faculty of Veterinary Medicine, Hokkaido University. My full-dress research on the pancreas was to investigate the effect of cholecystokinin (CCK) and its synthetic analogue caerulein on exocrine and endocrine pancreas using isolated perfused rat pancreas. I wrote and published several experimental studies in vivo and in vitro in the *Journal of Clinical Investigation* [Discrepancies between the doses of cholecystokinin or caerulein-stimulating exocrine and endocrine responses in perfused isolated rat pancreas. *J Clin Invest* 1979;63:478–484], *Endocrinology* [Effect of caerulein on exocrine and endocrine pancreas in the rat. *Endocrinology* 1979;105:1396–1399] and the *American Journal of Physiology* [Effects of porcine secretin on exocrine and endocrine function in the isolated perfused rat pancreas. *Am J Physiol* 1981;241:G43–G48].

From April 1980 to February 1982, I did my work with Professor John A. Williams at the Department of Physiology, University of California, San Francisco, as a Visiting Associate Professor of Medicine and Physiology. My main project at the University of California was about pancreatic exocrine function and CCK receptors in diabetes mellitus and I published several papers using isolated rat pancreatic acini in the *Journal of Clinical Investigation* [Effect of diabetes mellitus on the regulation of enzyme secretion by isolated rat pancreatic acini. *J Clin Invest* 1982;70:148–156] and *Gastroenterology* [Diabetes in the rat is associated with a reversible postreceptor defect in cholecystokinin action. *Gastroenterology* 1984;87:882–887].

M.E.F.-Z.: You have pioneered the pancreas research in so many directions. At the end of the day, what has given you the most personal satisfaction?

M.O.: Although I started pancreas research alone, I had opportunities to be the mentor of many fellows and engaged them in pancreatic research. This might be my greatest personal satisfaction. In addition, the personal relationship and friendship I developed with my colleagues in Japan as well as in foreign countries are a great personal satisfaction.

My scientific satisfaction is that I have achieved many projects that I started on pancreatic research such as amylase isoenzymes, the relationship between exocrine and

endocrine pancreatic functions, acute and chronic pancreatitis, and the mechanism of activation of isolated rat pancreatic satellite cells. Recent scientific satisfaction is that I am conducting a nationwide survey of acute and chronic pancreatitis in Japan, proposing diagnostic criteria for early chronic pancreatitis and autoimmune pancreatitis and guidelines for improvement of case fatality of severe acute pancreatitis as the chief investigator of the Research Committee of Intractable Pancreatic Diseases, provided by the Ministry of Health, Labour and Welfare in Japan. I have reported the nationwide survey work on acute and chronic pancreatitis at the 36th Annual Meeting of the American Pancreatic Association [Nationwide epidemiological survey of acute pancreatitis in Japan. *Pancreas* 2005;31:449; Nationwide epidemiological survey of chronic pancreatitis in Japan. *Pancreas* 2005;31:473].

M.E.F.-Z.: Based on your experience as mentee and mentor, can you comment on the value of mentorship in the development of new investigators?

M.O.: It is really very important. Unfortunately, however, I had no mentors when I started my research on the pancreas. My life itself might have changed had I had a good mentor when I started my research in this field. Having a good mentor can determine the direction and probability of success for a young researcher. Mentors should discuss with mentees and establish a regular review of progress. Mentors should also provide emotional support and encouragement. In addition, a mentor should attract mentees by his enthusiasm, excitement, and energy for science to research and keep them there.

M.E.F.-Z.: What advice can you give to young investigators starting in the field of pancreas research?

M.O.: At first it is important to be interested in everything related to the field and to search the assignments. Before starting research, field search is important. Research means repeats of search. Clinicians should indulge in research that aims to answer clinical questions and answer these questions in the laboratory. Once an investigational theme is formulated, the investigator should concentrate on that topic. Questions and hypotheses that arise during the research must be solved one by one. Research must not be ended as research, and is important to communicate the results obtained in the laboratory to the clinicians. The patients or research results that are different from those expected must be kept in mind. Research involving these unexpected patients or results may open the door and make great discoveries.

M.E.F.-Z.: What do you think are the big questions that need to be answered in the field of pancreatology?

M.O.: As a clinician, the important question is how to diagnose chronic pancreatitis at an early and reversible stage. Chronic pancreatitis is a disease characterized by progressive inflammation that results in irreversible fibrotic destruction of the pancreatic parenchyma, and exocrine and endocrine dysfunction. In contrast, however, fibrosis of the liver in patients with chronic hepatitis can be reversible after interferon therapy. The important question today is why chronic pancreatitis is an irreversible disease process?

Since chronic pancreatitis is known to occur in many different and clinically distinct forms, and since clinical features and presentations of chronic pancreatitis differ significantly, it seems inappropriate to lump all the different forms of chronic pancreatitis under a general clas-

sification and similar diagnostic criteria. The currently used diagnostic criteria for chronic pancreatitis can diagnose the terminal stage of chronic pancreatitis common to all etiologies, and thus chronic pancreatitis diagnosed by current criteria is irreversible. Accordingly, we have to invent new methods for the diagnosis of chronic pancreatitis at its reversible stage and prevent or resolve fibrosis of the pancreas. This may help to reduce pancreatic cancer resulting from chronic pancreatitis.

M.E.F.-Z.: What do you think is the major need that a journal like *Pancreatology* should fill?

M.O.: *Pancreatology* should publish peer-reviewed articles of high quality within 3–6 months after submission (or even earlier if possible), as well as commentaries of recent progress and reviews of educational contents.