

## Final Lecture

# A History of the Pan-Creas

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It is a great pleasure to see you here again, at this 6<sup>th</sup> SHOWA Pathology Seminar. The first Seminar was held on 2007 as memorial Ceremony of my 60-year-old birthday. Since then, this Seminar was warmly supported by many persons as you hear present.

Today, it is also a great honor, I can have a chance to speak as Special speech of this seminar and as my final lecture for my students, as an Active Professor.

Under the title of “A history of Pan-creas”, today I will focus on three episodes, concerning with Organogenesis, Discovery and Functions of the Pancreas.

## Episode One

The first, focusing on the mysteries concerning with organogenesis. The most interest point is, in spite of one organ, the pancreas is derived from two buds, originating from mid-gut.

Abdominal and Ventral bud are arising from mid-gut at the end of 4 weeks after fertilization, and Ventral bud turns behind of duodenum, and combine with ventral bud at the end of 7 weeks. Some malformations including Pancreatic Divisum and Anular Pancreas may be date back to this process (Fig. 1).

This work was performed with G. Koepfel, when we were young enough. Round pancreatic islets are scattered in Pancreatic body and tail, but the irregular islets are limiting at small area of the pancreatic head. Interestingly which are rich in PP-cell. We understood the phenomenon is one of the evidence of the fusion of both buds (Fig. 2).

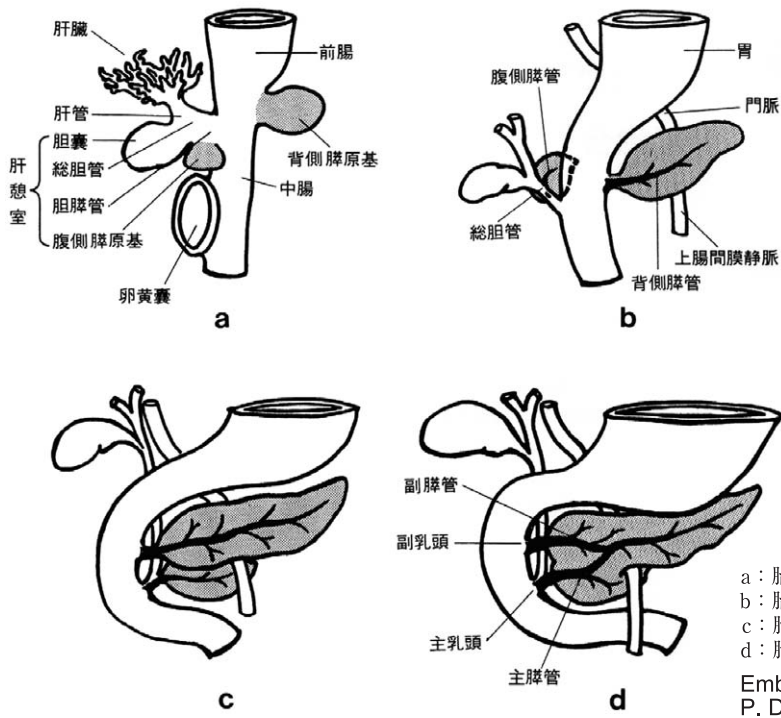
Embryologically, it is generally understood that endocrine Islets developed at 3 month gestational age, and begin to secrete at 5 month gestational age. Against, exocrine pancreas develops earlier, however, begin to secrete at post-natal term.

I will show you Interesting Mystery found in the perinatal exocrine pancreas. This is acinar cells of mice at the birth without any nutrition. Numerous number of enlarged zymogen granules fill in cytoplasm (Fig. 3).

Next, I will show you another type of acinar cells in the mice at the second day after birth with nutrition. You can clearly understand marked morphological differences between the perinatal exocrine pancreases. Then, we call fetal type and adult type of Acinar cells. This transforming seems to happen quickly in peri-natal term, turning from Fetal Type to Adult Type (Fig. 4).

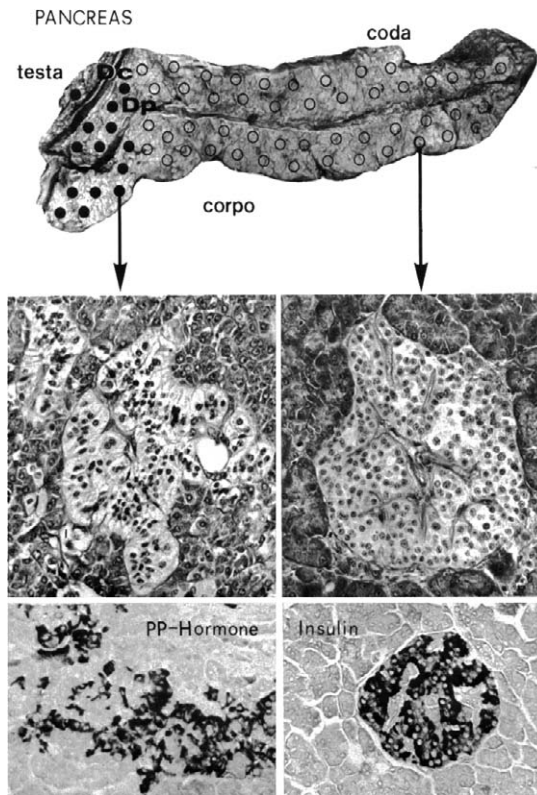
My idea about this transformation is follows.

As acinar cells is very dangerous, because which include numerous digestive enzymes, then, it's secretory-process should be strictly controlled, especially at peri-natal time. Against, they must



a : 胎生4週. 膵原基の形成  
 b : 胎生5週. 総胆管と腹側膵の回転の始まり  
 c : 胎生6週. 回転完了  
 d : 胎生7週. 腹側および背側膵の融合と両側膵管の癒合  
 Embryo-and Anatomical Aspect of  
 P. Divisum: N. Ohike *et al*, 1997

Fig. 1. 膵の発生



Aspetti Ultr. es Immunocit. del P.  
 Endocrino in Corso di Diabete:  
 G. Kloeppe *et al*, 1982

Fig. 2.

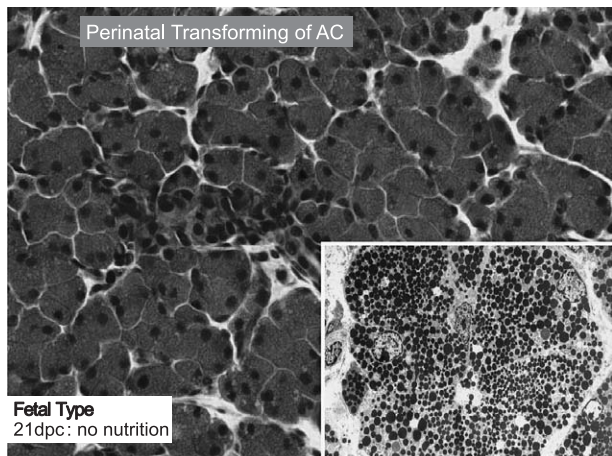


Fig. 3.

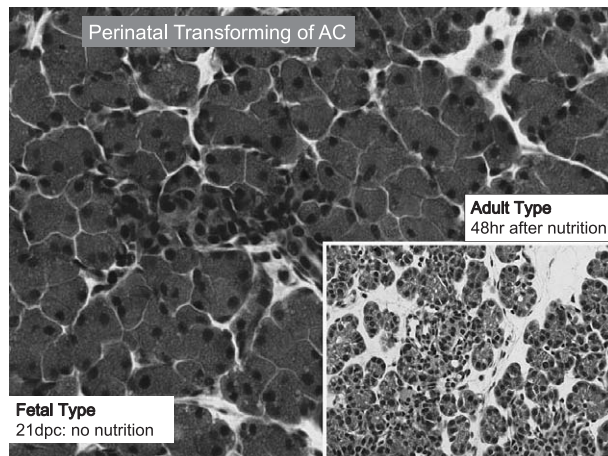


Fig. 4.

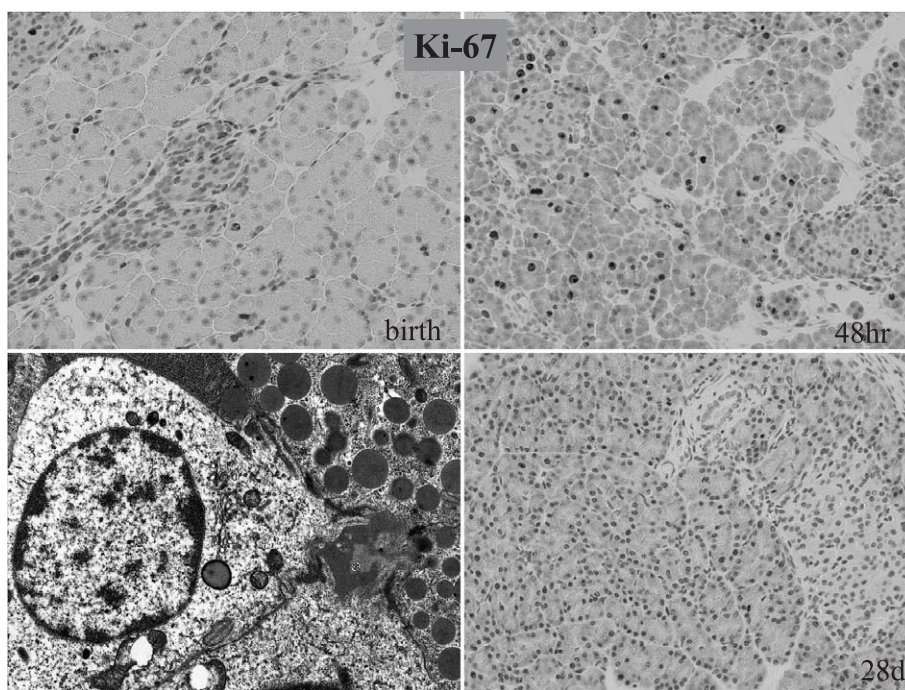


Fig. 5.

secrete more easily, after birth, to grow up quickly. The first nutrition may be a switch on this turning.

This examination was performed with Prof. Tajiri and his colleague. Ki-67 positive cells are most frequently observed 2 days after birth, and TUNNEL -method-positive cells are also more frequently observed on one or two day after birth. These facts may be supporting our idea about transforming. Ki-67-positive cells are corresponding to centro-acinar or intercalated cells, this is an electro-micro-scopical figure of which (Fig. 5).

This examination was performed with Prof. Kanda. In obstructive Pancreatitis, these mimic



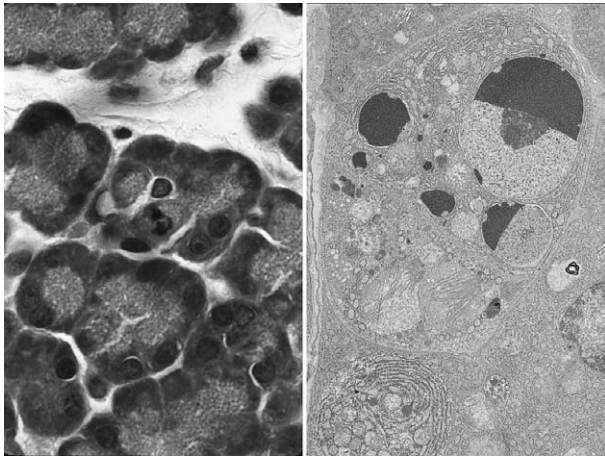


Fig. 6.

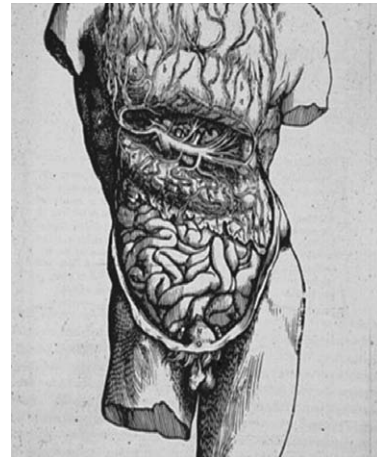


Fig. 7.



Fig. 8.

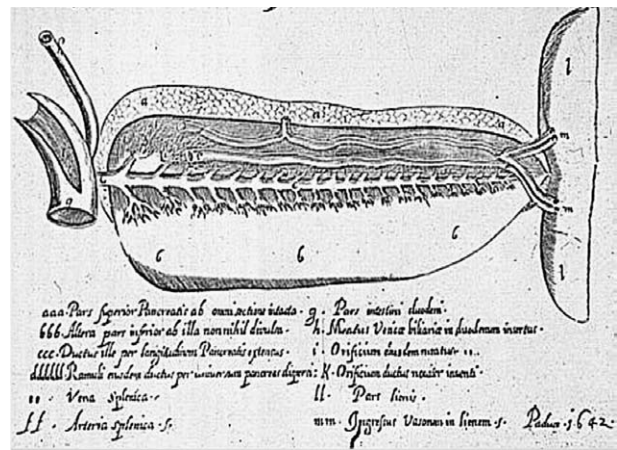


Fig. 9.

findings are often observed. The first we understood it as mitosis, however, but little later, terminally differentiated acinar cells can not regenerate. It is apoptosis, as you can see some apoptotic bodies (Fig. 6).

## Episode Two

The next, we will focus on the process of Discovery of the Organ Pancreas.

The words "Pancreas" is known since about 300 BC, but nobody could find till middle Ages. For example, this is an Atlas of abdominal lumen by Vesalius, *Faburica Anatomica*. Can you find pancreas (Fig. 7).

One day, I have a travel to a small village around the Sahara Desert, to visit a library, which is one of largest, storing more the 5000 Islamic antique books including medicine before 16 c. But there is no anatomical or pathological books describing about pancreas (Fig. 8).

This is famous figure showing Pancreas, recorded by Johann Georg Wirsung, when he had discovered main pancreatic duct, using feather of the wild duck, in 1672, in Padua (Fig. 9).



Fig. 10.



Fig. 11.

Three year ago, when I had visited Verona, Prof. Zammboni guided me to Padua, and we could find original cupper plate of this figure in the treasure-room of Padua-University.

Recently I am questioning on myself, who is the patron of the pancreas.

When I have drunk a little severe, probably Bear and whisky, got off the subway of London and finally found St. Pancras. But it is misunderstood, it is the name of the station of subway “St. Pancras”. Now I do not know who is St. Pancras, but when I visited Cort Dajule in France, when I visited Prof. Benoit, I have found many small villages named St. Pancras, but I could not found any St. Pancreas in France, too.

Moment I believe this is the Figure of St. Pancreas (Fig. 10), have you any question about it?

Dr. Wirsung is now sleeping at the main church in City Padua. At the time, more than 25,000 students were come from other foreign Cities in Europe to study at the leading medical center University Padua. He also came from Germany.

At the corner of the arch of the inside garden of the church, we can now find a memorial plate about him (Fig. 11). He was shot to death on 42 year old, but the reason is not known.

On the other hand, who is the first recorder about pancreas in Japan? This is the first Autopsy record, performed by Dr. Toyo Yamagata. He learned Chinese medicine. Can you find the pancreas on his record of the autopsy (Fig. 12). In that time, it is general believed that Human is consisted with five organs including heart, lung, liver, spleen and kidney. Thus, Chinese medicine includes no entity of the organ pancreas in that time.

This memorial stone (Fig. 13) is about second autopsy case, which was performed by a surgeon, Dr. Kohan Kuriyama. He was influenced by western medicine. He performed autopsy by himself and described about a mass of the upper abdominal lumen. According to the famous Anatomy-Prof. Teizo Ogawa, it should be the first record about pancreas in Japan. Now, you can see a small Budda behind the stone.

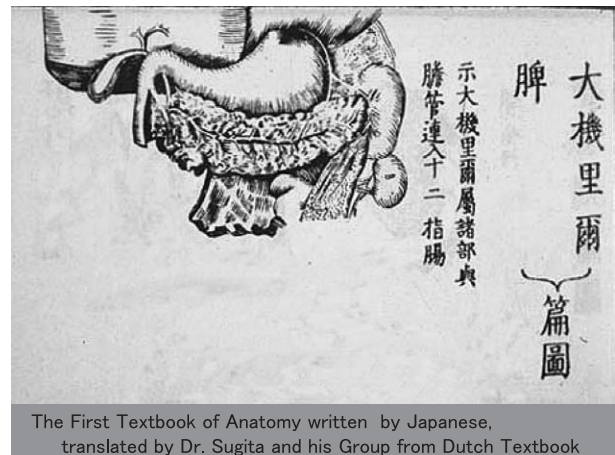
山脇東洋：  
1754解剖を見学、  
1759年、「臓志」を刊行



Fig. 12.



Fig. 13.



The First Textbook of Anatomy written by Japanese,  
translated by Dr. Sugita and his Group from Dutch Textbook

Fig. 14.

I believe this is St. Pancreas in Japan.

This is the first record about Pancreas in Japan (Fig. 14). This text book is translated form Dutch text book by Dr. Sugita and his Group. You can see here, pancreas, but not written as Pancreas in Japanese. In this Dutch texted book, it was written as Groot-kilie, not as Pancreas.

How do you think about this figure, which is drawn by Samurai painter learned western drawing-method. His name is Naotake Odano.

His home town is small in North Japan, but it is still good atmosphere of Edo-time.

Now, this is a Japanese-ward expressing pancreas. This ward is made by Dr. Udagawa (Fig. 15). He was well understood the ward Pancreas, and make a new ward. And this is the picture of



# 膵

was made by Dr. Udagawa in 18 C, he has understood the original meaning of pancreas:

Creas + Pan = 月 + 卒 = 膵

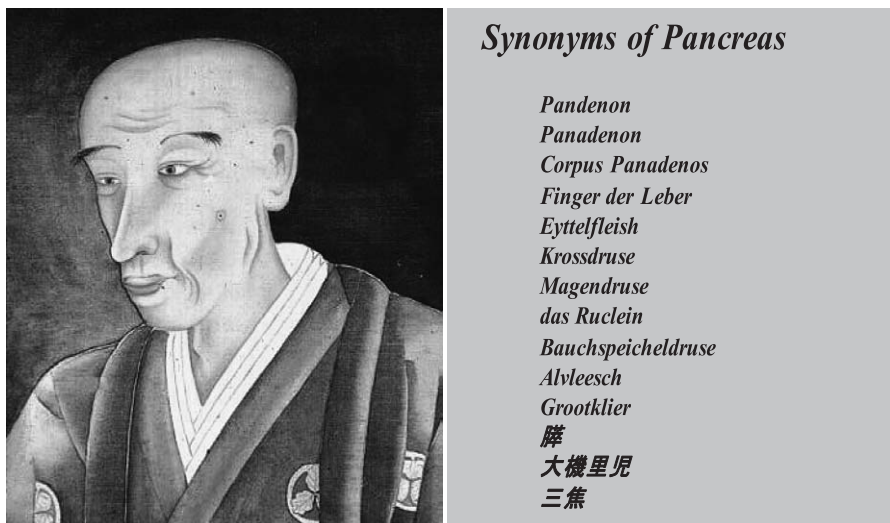


Fig. 15.

him. How do you think about him, is he handsome body. Yes, he is justly playboy and has many girl-friends. Therefore, he was a son-in-law of Dr. Sugita, but finally he was divorced.

## Episode Three

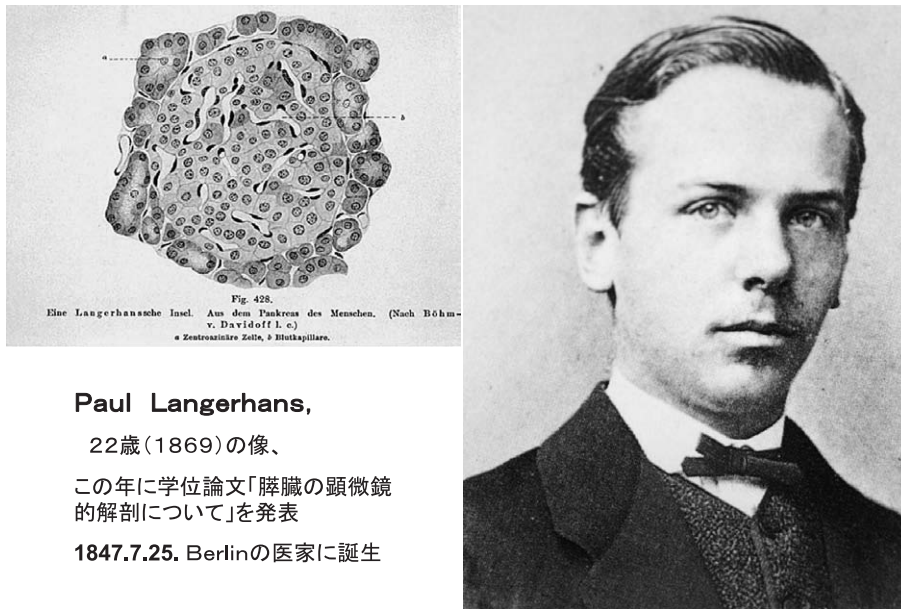
Next is Episode Three, concerning with the functions of the Pancreas.

What is the true meaning of the discovery of MPD? I think, it is a discovery of fifth humoral element. Before the Renaissance, European Medicine was strongly influenced by the humoral Pathology, based on four humoral elements including Sanguis, Phlegma, Melancholera and Cholera, which idea was established by Hyppcrate and Galenus. I think the most important point is to wake up over the Galenism.

On the other hand, it is well known that the pancreatic-islet was discovered by P. Langerhans, who was bone in Berlin, and a student of the famous Pathologist Prof. Virchow. I think he is really handsome boy, but I do not know how many girlfriends he had (Fig. 16).

He was died at the age of 41 year old by tuberculosis, similar age of the Wirsung's, at the small island Madeira in North-Atlantic Ocean, at very excellent wine is produced, named as Maderia. The function of pancreatic islet was not yet known when he died. It is known a little later in 20 C, by American research Group. It is a little comical that I heard the memorial stone of Langerhans is built by J. DM Association at the small cape of the island.

It is also known some mysterious pancreatic tumors showing both exocrine and endocrine characters, such as pancreatoblastoma, acinar cell carcinoma, and mixed exocrine-endocrine tumors, showing on the slide. About which, it is well described in recent WHO-blue book.



**Paul Langerhans,**

22歳(1869)の像、

この年に学位論文「膵臓の顕微鏡的解剖について」を発表

1847.7.25. Berlinの医家に誕生

Fig. 16.

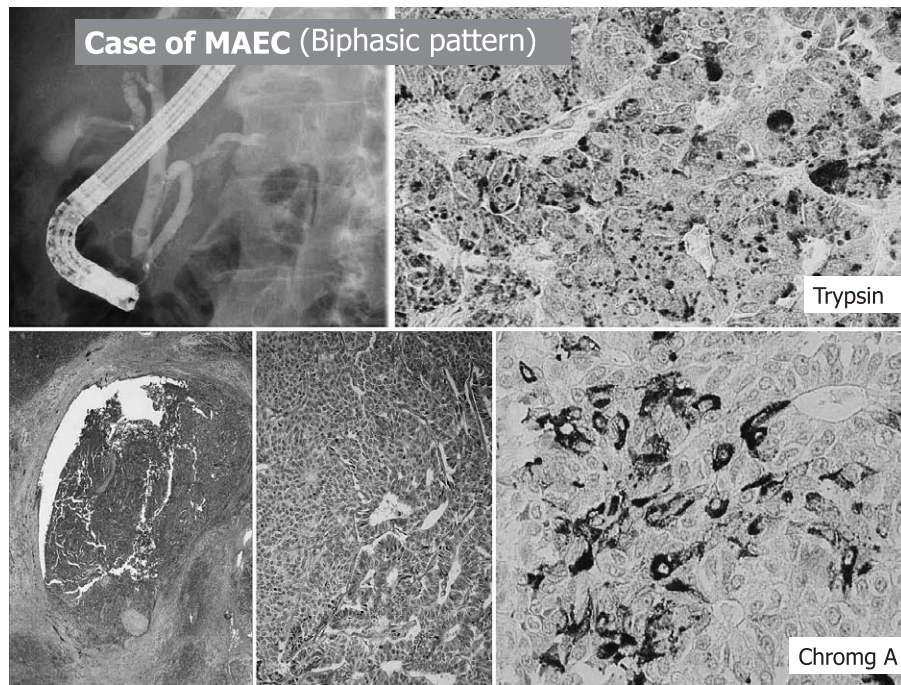


Fig. 17.

This is an examined-case of Mixed Exocrine-Endocrine Carcinoma (Fig. 17). Majority of tumor cells are positive for exocrine and endocrine markers.

This is mouse Pancreas. Multi-potential cells such as positive for PDX1 are recognized between duct-, acinar- and endocrine cells (Fig. 18). It may be understand these mysterious tumors are derived form those multi-potential cells.



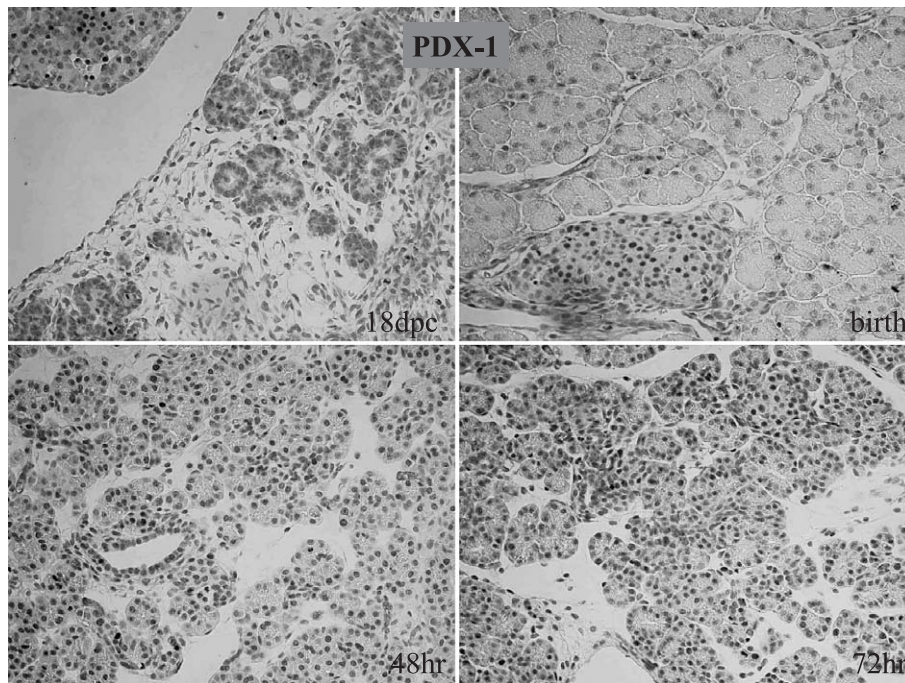


Fig. 18.

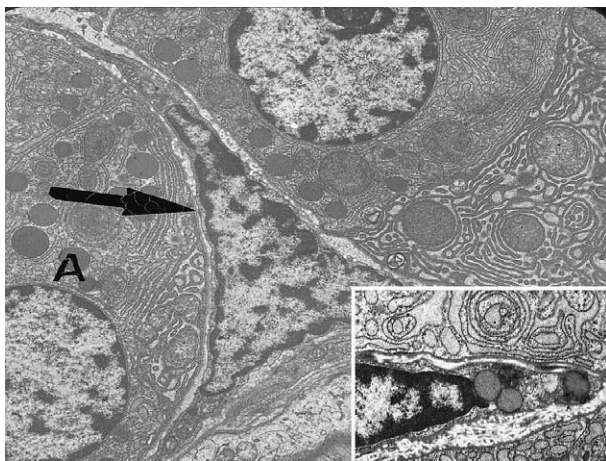


Fig. 19.



Fig. 20.

### Additional Episode

In order for your request, no request?. I will talk about additional one episode. More than 30 years ago, I have discussed with Prof. Becker in Erlangen-University. He was a leading Pathologist and Pancreatologist. He said me that alcoholic Pancreas is more frequently occurred in France, who likes to drink red-wine, and is not so frequently in Germany, because who likes to drink bear. And I had answered, Japanese likes to drink warm Sake, and alcoholic pancreas is very rare.

And, our result is, we must warm up alcohol at first, and then drink.

Additional he said, alcoholic disease will be more frequently happened in Japan, too.

When I had come back to Japan, my interest is about initial change of alcoholic pancreatitis. We found fine peri-cellular fibrosis owing spindlic peri-acinar cells, which are positive for alpha-SMA.

Electronmicroscopically, which cells include often lipovacuoli and produce collagen fibers (Fig. 19). About which finding we were discussed often with Prof. Suda and his Group.

This is final slid (Fig. 20). You can see here, St. Damian. The first, I believe he has an ink bottle at left hand, because he had a feather-pen on right hand. But he is a Patron in Catholicism, then, it is a medicine bottle. On the right slid, you can see a Buddha for medicine. He has also medicine-bottle on the hand. However, recently I have suddenly recognized, which are decanters of red- or white wine, or Sake. Then, I can finally found out they are justly the Patron for alcoholic diseases.

Thank you for your warmly attentions.