

This Week's Citation Classic

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Lacy P E & Kostianovsky M. Method for the isolation of intact islets of Langerhans from the rat pancreas. *Diabetes* 16:35-9, 1967. [Dept. Pathology, Washington Univ. Sch. Med., St. Louis, MO]

The paper describes a simple method for the isolation of intact, viable islets from the normal rat pancreas for *in vitro* studies on hormonal secretion. The method was based upon disruption of the exocrine pancreas prior to digestion of the tissue with collagenase. [The SCI® indicates that this paper has been cited over 685 times since 1967.1

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"The islets of Langerhans are nests of endocrine cells which are scattered throughout the pancreas and comprise only a few percent of the entire organ. This anatomical fact placed a severe limitation on studies concerned with the mechanisms for stimulation and secretion of islet hormones. In our early studies on the ultrastructural events involved in insulin secretion, we attempted to circumvent the problem by serially sectioning blocks of pancreas until an islet was found. In order to correlate enzymatic changes in the islets with insulin secretion, we dissected islets from frozen-dried sections of pancreas, weighed the tissue on a quartz fiber balance and used it for quantitative enzymatic studies. Obviously, these approaches were extremely tedious and frustrating and provided new but yet limited information. Further progress required the development of a simple means for isolating viable islets for *in vitro* studies on hormonal secretion.

"In 1965, Moskalewski¹ reported that islets could be isolated by partial digestion of the guinea pig pancreas with collagenase. We tried the procedure and soon found that it did not provide a reproducible means of isolating viable islets in sufficient quantities for *in vitro* studies. In considering different approaches for improving the procedure, we knew that the exocrine portion of the pancreas was drained by ducts, whereas the islets were not associated with the ductal system. Therefore, it seemed logical to attempt to inject saline into the pancreatic duct in order to disrupt the exocrine pancreas prior to digesting it with collagenase. This is one of the rare instances where logic produced the expected results and a simple reproducible procedure was developed for the rapid isolation of viable islets for *in vitro* studies on hormonal secretion.

"This procedure for islet isolation quickly became a vital tool in our own investigations on the mechanism of glucose-induced insulin secretion. Utilizing isolated islets maintained *in vitro*, we were able to demonstrate that the microtubular-microfilament system of the beta cell was involved in insulin release following stimulation with glucose. Subcellular fractions of the islets were isolated and procedures were developed for obtaining a plasma membrane fraction for studies on the mechanism of recognition of glucose by beta cells. Isolated islets have also been used for studies on insulin synthesis, proinsulin synthesis, glucagon synthesis and secretion, morphology of the plasma membrane of islet cells, hexose and calcium transport, membrane potential of beta cells, and transplantation of islets into diabetic recipients.

"The diverse application of this procedure to many different problems would probably explain why this paper achieved the most-cited' list. From my standpoint, I am delighted that a logical conjecture in research was successful, and I am grateful to learn that others were also assisted in their studies on the endocrine pancreas."

1. Moskalewski S. Isolation and culture of the islets of Langerhans of the guinea pig. *Gen. Comp. Endocrinol.* 5:342-53, 1965.