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| NAME  Gaisano, Herbert Y | | POSITION TITLE  Professor, Medicine and Physiology | | |
| eRA COMMONS USER NAME | |  | | |
| EDUCATION/TRAINING | | | | |
| INSTITUTION AND LOCATION | DEGREE | | YEAR(s) | FIELD OF STUDY |
| University of the Philippines, Manila | B. Sci. | | 1974-1977 | Pre-Medicine |
| University of the Philippines, Manila | M.D. | | 1977-1981 | Medicine |
| Mayo Clinic, Rochester, Minnesota | Res. Fellow | | 1983-1984 | Pancreatic research |
| Mayo Clinic, Rochester, Minnesota  Mayo Clinic, Rochester, Minnesota | Residency  Fellowship | | 1984-1986  1986-1990 | Internal Medicine  GI, Research |

**A. Personal Statement (referenced to Section C)**

I was one of the first to translate the thinking of SNARE protein regulation of neurosecretion to non neuronal cells to regulate secretion by showing that VAMP-2 mediated pancreatic acinar enzyme secretion (14). This study raised the possibility that other synaptic SNAREs might belong to large gene families which include non-neuronal members, which resulted in the "explosion" of the SNARE field in non-neuronal cell biology. We discovered acinar isoforms of VAMP-2,-3, Syntaxins -2, -3,-4, and SNAP-23 (16-18), which form combinations of complexes that localized to distinct membrane compartments of a single epithelial acinar cell to mediate distinct exocytic processes (22,24,25,28,35). We found that Munc18c binds basal membrane Syntaxin-4 to prevent it from forming a complex with SNAP-23 and VAMP-2, which would consummate basolateral exocytosis, which we postulated to be a mechanism of acute pancreatitis (28,69) and chronic pancreatitis (44); and then found VAMP8 to be the putative v-SNARE for basolateral exocytosis (95).We have now applied this model to in part explain the molecular mechanism of alcoholic pancreatitis (72,73,74), which was funded by the Alcohol Beverage Medical Research Foundation, NIH, and U.S. Department of Defense. We further clarified the molecular mechanism of physiologic apical exocytosis, including the role of Munc18b (in prep) and a novel interacting protein Cab45b (79). This work has modified the way the pancreatic scientific community now thinks of the molecular bases of regulated exocytosis and pathologic exocytosis underlying pancreatitis (24,28,69,103); and has resulted in national and international Young Investigator Awards, an Associate Editorship in the journal Pancreas. I was the first non-American to receive a Scholarship from the Amer. GI Association; and most recently, I was award the Canadian Association of Gastroenterology Research Excellence Award (highest award). We developed adenoviral gene transfer methods to introduce SNARE mutant genes into acinar cells (22) maintained in long-term culture to elucidate the structure-function of the SNARE proteins (25). Using these assays, we are now examining the specific actions of Syntaxin-2 and -3 and the interacting Munc18b in controlling the apical exocytic events (79). We have now further developed the exocytosis imaging assays to now include spinning disc confocal microscopy (125), multi-photon microscopy (128) and evanescent microscopy (total internal reflection fluorescence microscopy). Lastly, we developed a true in situ strategy to examine the exocrine pancreas by very fine slicing of pancreas in rodents wherein we first employed to examine islet cell function (119), and now applied to examine acinar biology (this proposal) deploying the various mentioned imaging assays.

**B. Positions and Honors.**

**Current Positions:**

2004- Professor, Departments of Medicine and Physiology, University of Toronto

1991 - present Staff Physician, Division of Gastroenterology, University Health Network of Toronto

1994 - present Faculty Member, Institute of Medical Science, University of Toronto, Faculty of Graduate Studies

**Previous Positions:**

1991 - 1998 Assistant Professor, Department of Medicine, University of Toronto

1996 - 1998 Assistant Professor, Department of Physiology, University of Toronto

1998 – 2004 Associate Professor, Departments of Medicine and Physiology, University of Toronto

1996 – 2003 Research Director, Division of Gastroenterology, University Health Network of Toronto

**Professional Activities:**

2006- Editorial Board, Journal of Biological Chemistry

1997 **-** present Associate Editor, Pancreas (Journal),

2000 - 2003 Juvenile Diabetes Research Foundation, Medical Science Review Committee

2004-present Canadian Institute for Health Research internal review committees (Cell Physiology, DOL, Exp.

Med)

**Honors and Awards:**

1994 American Gastroenterology Association / Industry Research Scholar Award

1994 Young Investigator Award, Intl Assn.of Pancreatology / American Pancreatic Association

1997 Young Investigator Award, Canadian Association of Gastroenterology

2003 Mary Jane Kugel Award, Juvenile Diabetes Research Foundation

2010 Canadian Association of Gastroenterology Research Excellence Award

**C. Publications (in chronological order- from most recent, 15 selected publications pertaining to exocrine research). Lifetime: 130 papers**

128. Behrendorff, N, Dolai S, Hong W, **Gaisano HY**,Thorn P. VAMP 8 is a SNARE selectively required for sequential granule-to-granule fusion ***. J. Biol. Chem.*** 286(34):29627-34, 2011

125. Fernandez N, Liang T, **Gaisano HY.** Live Pancreatic Acinar Imaging of Exocytosis Using Syncollin-pHluorin. ***Amer. J. Physiol. Cell Physiol.***  300(6):C1513-23, 2011

119. Huang YC, Rupnik M, **Gaisano HY**. Unperturbed islet alpha-cell function examined in mouse pancreatic tissue slices. ***J. Physiology*** 589(Pt 2):395-408, 2011

103. **Gaisano HY**, Gorelick F. New Insights into Mechanisms of Acute Pancreatitis. ***Gastroenterology*** 136(7):2040-4, 2009

95. Cosen-Binker L, Binker MG, Wang CC, Hong W, **GaisanoHY**. VAMP8 is the v-SNARE mediating basolateral exocytosis in alcoholic pancreatitis. ***J. Clin. Invest.*** 118(7):2535-51, 2008.

79. Lam PPL, HyvärinenK, Kauppi M, Cosen-Binker L, Saara Laitinen S, Sirkka Keränen S, **Gaisano HY**, Olkkonen VM. A Cytosolic Splice Variant of Cab45 Interacts with Munc18b and Impacts on Amylase Secretion by Pancreatic Acini. ***Molec. Biol. Cell*** 18(7):2473-80, 2007

74. Lam PPL, Cosen-Binker L, Lugea A, Pandol S, **Gaisano HY**. Alcohol redirects CCK –mediated apical exocytosis to pancreatic acinar basolateral membrane in alcoholic pancreatitis. ***Traffic*** 8(5):605-17, 2007.

73. Cosen-Binker L, Lam PPL, Binker M, Reeves J, Pandol S, **GaisanoHY**. Alcohol/cholecystokinin-evoked pancreatic acinar basolateral exocytosis is mediated by PKCα phosphorylation of Munc18c**. *J. Biol. Chem.*** 282(17):13047-58, 2007

72. Cosen-Binker LI, Lam PPL, Binker MG, **GaisanoHY**. Alcohol-induced PKC alpha phosphorylation of Munc18c in carbachol-stimulated acini causes ectopic basolateral exocytosis. ***Gastroenterology*** 132(4):1527-45, 2007

69. Cosen-Binker LI, **Gaisano HY**. Recent insights into the cellular mechanisms of acute pancreatitis. ***Can. J. Gastro***. 21(1):19-24, 2007

44. **Gaisano HY**, Sheu L, Whitcomb D. Alcohol chronic pancreatitis involves displacement of Munc18c from the pancreatic acinar basal surface. ***Pancreas*** 28(4):395-400, 2004

28. **Gaisano HY**, Lutz M, Leser J, Sheu L, Lynch G, Tang L, Tamori Y, Trimble WS, Salapatek AM.

Supramaximal CCK redirects exocytosis from the apical to the basal plasma membrane in rat pancreatic acinar cells involving displacement of Munc18c from the basal membrane. ***J. Clin. Invest.*** 108:1597-1611,2001

25. Huang XH, Sheu L, Tamori Y, Trimble WS, **Gaisano HY.** CCK-regulated exocytosis in rat pancreatic acinar cells is inhibited by a C-terminus truncated mutant of SNAP-23. ***Pancreas*** 23, 125-133, 2001

17. **Gaisano HY,** Ghai M, Sheu L, Bouquillon A, Bennett MK, and Trimble WS. Distinct locations of the syntaxin family of proteins in rat pancreatic acinar cells***. Molec. Biol. Cell*** 7:2019-2027, 1996.

16. **Gaisano HY**, Sheu L, Grondin G, Ghai M, Bouquillon A, Beaudoin A, Lowe A, Trimble WS. The VAMP family in pancreatic and parotid acinar cells. ***Gastroenterology*** 111:1661-1669, 1996.

14. **Gaisano HY**, Sheu L, Foskett JK and Trimble WS. Tetanus toxin-light chain cleaves a vesicle-associated membrane protein (VAMP) isoform 2 in rat pancreatic zymogen granules and inhibits enzyme secretion. ***J. Biol. Chem.*** 269:17062-17066, 1994.