BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Pauline Kay Lund	Professor
eRA COMMONS USER NAME (credential, e.g., agency login)	
kay_lund	

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Newcastle upon Tyne	B. Sc. Hons.	1975	Physiology
University of Newcastle upon Tyne	Ph.D.	1979	G.I. Endocrinology
Massachusetts General Hospital and Harvard Medical School (Joint)	Postdoctoral Res. Fellow	1979-82	Recomb. DNA Glucagon Biosynthesis

A. Personal Statement

Dr. Lund has made major contributions to defining the regulation of intestinal growth by insulin/insulin-like growth factor family of receptors and enterotrophic hormones. She was the first to clone the proglucagon gene and identify new intestinal hormones, glucagon-like peptide 1 (GLP1; under clinical trial in diabetes) and glucagon-like peptide 2 (GLP2; under trial as a trophic therapy in the GI tract). She has made major contributions to understanding how IGF/insulin and downstream signaling pathways regulate normal and aberrant growth of intestinal epithelium and their roles in intestinal cancer. Her current research focuses on dissecting the roles of IGF1R versus two insulin receptor isoforms (IR-A or IR-B) in obesity-associated tumorigenesis and in normal and tumor-derived intestinal stem cells. In other research, Dr. Lund defined suppressors of cytokine signaling (SOCS) as tumor suppressors and is currently exploring their roles in inflammatory bowel disease (IBD) associated colon cancer, stem cells and inflammation-induced fibrosis. Recent novel findings from the Lund Lab that high-fat diet: bacteria interactions promote intestinal inflammation during development of obesity. This led to recent collaborations with the lab of Jenny Ting to explore how nod-like receptors (NLRPs) and effector may impact diet-associated intestinal inflammation or the effect of obesity to promote precancerous adenomas or CRC. Other ongoing research addresses molecular and cellular mechanisms of fibrosis in inflammatory bowel disease and crosstalk between intestinal mesenchymal cells and intestinal epithelial stem cells during repair after injury.

A new area of research addresses the role of aging in intestinal stem cells during normal renewal of intestinal epithelium or regeneration after injury. This research tests the hypothesis that IGF/IGF1R signal promotes intestinal stem cell aging and dysfunction while preserved insulin/insulin receptor signaling protects against aging induced dysfunction of stem cells or intestinal epithelium.

Dr. Lund is a member of the Center for Gastrointestinal Biology and Disease, the Lineberger Comprehensive Cancer Center and the Neurobiology Curriculum. She has active collaborations with the Intestinal Stem Cell Group (Scott Magness, Susan Henning, Chris Dekaney), Robert Sandler, Temitope Keku (CGIBD and Medicine) and Jenny Ting (Microbiology and Immunology).

B. Positions and Honors

Professional Experience

1982-1988 Assistant Professor in Physiology (tenure track), UNC-Chapel Hill
1988-1993 Associate Professor in Physiology (tenured), UNC-Chapel Hill
1995-1996 Senior research fellow, Ludwig Institute for Cancer Research
1995-1998 Professor of Distinguished Teaching (Named Chair), UNC-Chapel Hill
1998-present Professor of Nutrition, UNC-Chapel Hill
1993-present Professor of Cell & Molecular Physiology and Pediatrics (tenured), UNC-Chapel Hill
2007-present Sarah Graham Kenan Professor of Cell & Molecular Physiology, UNC-Chapel Hill

Awards AGA Research Mentor Award, 2012; University Award for the Advancement of Women, 2008; Dean's Medical School Teaching Excellence Award, 2002; Freshman Medical Class Teaching Award, 1998, 1994,

1993, 1990; University Professor of Distinguished Teaching, 1995; Hyman L. Battle Medical Teaching Award, 1994; Kaiser Permanente Teaching Award, 1994; Ruth and Paul Hettleman Award for Scholarly Research, 1990

Professional Duties: Member NIH Clinical and Integrated Molecular Gastroenterology Study Section; **Associate Editor** Gastroenterology 2001-2006; **Member** American Gastroenterology Association Research Policy Committee 2004-2005; **Co-Director** CGIBD Gnotobiotic Rodent Facility, UNC; **Editor in Chief** American Journal of Physiology, Gastrointestinal and Liver 2009-present

C. Selected Peer-reviewed Publications

1. Martin C, Connelly A, Keku TO, Mountcastle SB, Galanko J, Woosley JT, Schliebe B, **Lund PK**, Sandler RS. NSAIDs, apoptosis, and colorectal adenomas. Gastroenterology 2002; 123(6):1770-7. PMID: 12454832. PMC in process.
2. Miller ME, Michaylira CZ, Simmons JG, Ney DM, Dahly EM, Heath JK, **Lund PK**. Suppressor of cytokine signaling-2: a growth hormone inducible inhibitor of intestinal epithelial cell proliferation. Gastroenterology 2004; 127(2):570-81. PMID: 15300589. PMC in process.
3. Theiss AL, Fuller CR, Simmons JG, Liu B, Sartor RB, **Lund PK**. Growth hormone reduces the severity of fibrosis associated with chronic intestinal inflammation. Gastroenterology 2005; 129(1):204-19. PMID: 16012948. PMC in process.
4. Keku TO, **Lund PK**, Galanko J, Simmons JG, Woosley JT, Sandler RS. Insulin resistance, apoptosis and colorectal adenoma risk. Cancer Epidemiol Biomarkers Prev 2005; 14(9):2076-81. PMID: 16172212. PMC in process.
5. Theiss AL, Simmons JG, Jobin C, **Lund PK**. Tumor necrosis factor (TNF) alpha increases collagen accumulation and proliferation in intestinal myofibroblasts via TNF receptor 2. J Biol Chem 2005; 280(43):36099-109. PMID: 16141211. PMC in process.
6. Michaylira CZ, Ramocki NM, Simmons JG, Scull BP, Tanner CK, McNaughton KK, Fuller CR, Woosley JT, Greenhalgh CJ, **Lund PK**. Haplotype insufficiency for SOCS2 enhances intestinal growth and promotes polyp formation in GH-transgenic mice. Endocrinology 2006; 147(4):1632-41. PMID: 16410303. PMC in process.
7. **Lund PK**, Rigby RJ. SOC-ing it to tumors: suppressors of cytokine signaling as tumor repressors. Gastroenterology 2006; 131(1):317-9. PMID: 16831614. PMC in process.
8. Rigby RJ, Simmons JG, Greenhalgh CJ, Alexander WS, **Lund PK**. Suppressor of cytokine signaling 3 (SOCS3) limits damage-induced crypt hyper-proliferation and inflammation-associated tumorigenesis in the colon. Oncogene 2007; 26(33):4833-41. PMID: 17297444. PMC in process.
9. Dekaney CM, Fong JJ, Rigby RJ, **Lund PK**, Henning SJ, Helmrath MA. Expansion of intestinal stem cells associated with long-term adaptation following ileo-cecal resection in mice. Am J Physiol Gastrointest Liver Physiol 2007; 293(5):G1013-22. PMID: 17855764. PMC in process.
10. Ramocki NM, Wilkins HR, Magness ST, Simmons JG, Scull BP, Lee GH, McNaughton KK, **Lund PK**. Insulin receptor substrate-1 deficiency promotes apoptosis in the putative intestinal crypt stem cell region, limits $APC^{Min/+}$ tumors, and regulates Sox9. Endocrinology 2008; 149(1):261-7. PMID: 17916629. PMCID: PMC2194604.
11. Zhang H, Morgan D, Cecil G, Burkholder A, Ramocki N, Scull B, **Lund PK**. Biochromoendoscopy: molecular imaging with capsule endoscopy for detection of adenomas of the GI tract. Gastrointest Endosc 2008; 68(3):520-7. PMID: 18499106. PMCID: PMC2754293.
12. Keku TO, Sandler RS, Simmons JG, Galanko J, Woosley JT, Proffitt M, Omofoye O, McDoom M, **Lund PK**. Local IGFBP-3 mRNA expression, apoptosis and risk of colorectal adenomas. BMC Cancer 2008; 8:143. PMID: 18498652. PMCID: PMC2409350.
13. Garrison AP, Dekaney CM, von Allmen DC, **Lund PK**, Henning SJ, Helmrath MA. Early but not late administration of glucagon-like peptide-2 following ileo-cecal resection augments putative intestinal stem cell expansion. Am J Physiol Gastrointest Liver Physiol 2009; 296(3):G643-50. PMID: 19118113. PMCID: PMC2660180.
14. Rigby RJ, Hunt MR, Scull BP, Simmons JG, Speck KE, Helmrath MA, **Lund PK.** A new animal model of post-surgical bowel inflammation and fibrosis: the effect of commensal microflora. Gut 2009; 58(8):1104-12. PMID: 19398439. PMCID: PMC2752281.

15. Newton VA, Ramocki NM, Scull BP, Simmons JG, McNaughton K, **Lund PK.** Suppressor of cytokine signaling-2 gene disruption promotes $Apc^{Min/+}$ tumorigenesis and AP-1 activation. Am J Pathol 2010; 176(5):2320-32. PMID: 20348236. PMCID: PMC2861097.
16. Hamilton KE, **Lund PK**, Galanko JA, Sandler RS, and Keku TO. Suppressor of cytokine signaling 3 (SOCS3) is not an independent biomarker of colorectal adenoma risk. BMC Res Notes 2010; 25;3:144. PMID: 20500855. PMCID: PMC2883989.
17. Ding S, Chi MM, Scull BP, Rigby R, Schwerbrock NMJ, Magness S, Jobin C, **Lund PK.** High-fat diet: bacteria interactions promote intestinal inflammation which precedes and correlates with obesity and insulin resistance in mouse. PLoS One 2010; 5(8):e12191. PMID: 20808947. PMCID: PMC2922379.
18. Speck KE, Garrison AP, Rigby RJ, von Allmen DC, **Lund PK,** and Helmrath MA. Inflammation enhances resection-induced intestinal adaptive growth in IL-10 null mice. J Surg Res 2011; 168(1):62-9. PMID: 20074747. PMCID: PMC2889031.
19. Hamilton KE, Simmons JG**,** Ding S, Van Landeghem L, **Lund PK**. Cytokine induction of tumor necrosis factor receptor 2 is mediated by STAT3 in colon cancer cells. Mol Cancer Res 2011; 9(12):1718-31. PMID: 21994466. PMCID: PMC3243771.
20. Leen JL, Izzo A, Upadhyay C, Rowland KJ, Dubé PE, Gu S, Heximer SP, Rhodes CJ, Storm DR, **Lund PK,** Brubaker PL. Mechanism of action of glucagon-like peptide-2 to increase IGF-1 mRNA in intestinal subepithelial fibroblasts. Endocrinology 2011; 152(2):436-46. PMID: 21159855. PMCID: PMC3384785.
21. Ding S, **Lund PK**. Role of intestinal inflammation as an early event in obesity and insulin resistance. Curr Opin Clin Nutr Metab Care 2011; 14(4):328-33. PMID: 21587067. PMCID in process.
22. Bortvedt SF, **Lund PK**. Insulin-like growth factor 1: common mediator of multiple enterotrophic hormones and growth factors. Curr Opin Gastroenterol 2012; 28(2):89-98. PMID: 22241077. PMC in process.
23. Van Landeghem L, Santoro AM, Krebs AE, Gracz A, Dehmer JJ, Scull BP, McNaughton K, Magness ST, **Lund PK.** Activation of two distinct Sox9-EGFP expressing intestinal stem cell populations during crypt regeneration after irradiation. Am J Physiol Gastrointest Liver Physiol. 2012; 302(10):G1111-32. PMID: 22361729. PMCID: PMC3362093.
24. Ding S, Walton KLW, Blue ER, McNaughton K, **Lund PK**. Mucosal healing and fibrosis after acute or chronic inflammation in wild type FVB-N mice and C57BL6 procollagen (<alpha>1) I-promoter-GFP reporter mice. PLoS One. 2012;7(8):e42568. PMID: 22880035. PMCID: PMC3411826.
25. **Lund PK**. Fixing the Breaks in Intestinal Stem Cells After Radiation: A Matter of DNA Damage and Death or DNA Repair and Regeneration. Gastroenterology 2012. Published ahead of print. PMID 23000480.
26. Ding S, Blue RE, Chen Y, Scull BP, **Lund PK**, Morgan DR. Molecular imaging of gastric dysplasia with near infrared fluorescence (NIRF). Molecular Imaging, 2012. Accepted for publication.

D. Research Support

ACTIVE

1-R01-AG041198-01A1 (PI Lund) 8/1/12-6/30/17
NIH
Aging, Intestinal Stem Cells and Insulin/IGF system
This project will identify the receptors that mediate effects of insulin or IGFs on intestinal epithelial stem cells (IESC) and renewal and repair of the epithelial lining of the intestine over the course of normal aging. Aim 1 will define the molecular and functional effects of aging on normal and regenerating IESC, progenitors and differentiated cells. Aim 2 will test the hypothesis that loss of intestinal epithelial IR promotes excessive IGF-IR signaling and accelerates aging-associated dysfunction of IESC, progenitors, EEC or other differentiated IEC. Aim 3 will test the hypothesis that loss of intestinal epithelial IGF-IR delays or attenuates IESC or intestinal epithelial aging.

5-R01-DK040247-19 (PI Lund) 7/28/11 – 6/30/15
NIH/NIDDK
Intestinal Adaptation-Role of Hormones and Growth Factors
The specific aims of this project are: 1) to define the specific effects of intestinal epithelial deletion of IGF-IR on intestinal tumorigenesis and hormone-induced growth; 2) to define the effects of intestinal epithelial deletion of IR on intestinal tumorigenesis and hormone-induced growth; 3) to define whether IGF-IR or IR mediate the effects of high fat diet (HFD)-induced hyperinsulinemia and obesity on intestinal growth or tumorigenesis.

5-R01-DK047769-12 (PI Lund) 7/1/09 – 3/31/14
NIH/NIDDK
Growth Factors and Inflammatory Bowel Disease
This proposal will test a central hypothesis that intestinal epithelial cell (IEC)-derived suppressor of cytokine signaling-3 (SOCS3) protects against crypt hyperplasia, dysplasia and neoplasia during chronic intestinal inflammation. Aim 1 will define cellular mechanisms and molecular targets of SOCS3 in the AOM model of inflammation-associated colon cancer; Aim 2 will define cellular and molecular mechanisms regulated by SOCS3 in colon cancer cells in culture with a focus on STAT3, TNFR2 and NFkB and Aim 3 will define if IEC-SOCS3 deletion promotes dysplasia in the IL-10 null model of IBD.

5-K12-GM000678-14 (PI Dykstra, Co-PI Lund)
NIH/NIGMS 9/1/12 – 8/31/17
Seeding Postdoctoral Innovators in Research and Education (SPIRE)
Goals: The SPIRE program is an Institutional Research and Academic Career Development Award (IRACDA) for postdoctoral fellows in the biomedical sciences, delivered through the University of North Carolina at Chapel Hill in partnership with four historically minority universities within the state of North Carolina. The program provides postdoctoral fellows with research training as well as professional development and a year of hands-on teaching experience at minority-serving undergraduate institutions.

5-U01-D085547-03 (PI Henning) 9/30/09 – 8/31/14
NIH/NIDDK
Collaborative Approaches to the Study of Intestinal Epithelial Stem Cells
Goal: to improve isolation methods for ISC by the identification of suitable membrane antigens fir antibody sorting and to use functional properties to separate active quiescent ISC. Dr. Lund is co-investigator. Her role is to establish a mouse model of radiation-induced intestinal stem cell ablation in an isolated intestinal segment for tests of stem cell transplantation in models of impaired stem cell regeneration.

5-U01-CA105417-08 (PI Threadgill, NC State 9/1/09 – 7/31/14
University; P.I. Pomp, sub-contract at UNC)
NIH/NCI
Modeling Heterogeneity for Safe Cancer Prevention and Detection
This project focuses genetic background effects in mouse models of colorectal cancer or environmental modifiers of colorectal cancer risk. Dr. Lund is co-investigator, focusing on applying and developing activatable probes to detect and quantify tumors and microadenomas. Support to Lund Lab includes funds for one postdoctoral trainee (Shengli Ding, PhD).