

MEDICAL STUDENT SUMMER RESEARCH PROGRAM AND RESEARCH THESIS PROGRAM MENTOR INFORMATION:

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1) Research description:

- a) General research description
- b) Description of potential MSSRP or RTP projects.

a) Pathogenesis of necrotizing enterocolitis and developmental regulation of the inflammatory response.

Dr. De Plaen's research focuses on how inflammation is regulated in the neonatal intestine and how the immaturity of the inflammatory response might contribute to necrotizing enterocolitis, a devastating disease of the premature infant, causing sudden bowel inflammation and necrosis. Her laboratory focuses on studying the developmental differences in the regulation of pro-inflammatory cytokines and in the activation of the transcription factor nuclear factor- κ B (NF- κ B), a key regulator of the inflammatory response, in the intestine during development. She is using a neonatal mouse model of NEC induced by hypoxia-cold stress-formula feedings that was developed in her lab and several transgenic mice with cell-specific deletion of IKK β , the upstream kinase responsible for NF- κ B activation. She is also studying how tight junction disruption contributes to NEC in this model.

b) Ongoing projects are:

- Determine cytokine gene expression in NEC and the contribution of NF- κ B activation in specific cell types.
- Study intestinal epithelial apoptosis in NEC and the role of NF- κ B activation in specific cell types.

Project ongoing in the lab uses several techniques such as laser capture microscopy, real time-PCR, western blot, ELISA, immunochemical and immunofluorescence studies.

2) Reasons for my interest in becoming a mentor:

- I believe our laboratory offers a unique experience in the field of translational research to any medical student who wants to invest time in research. Our laboratory has welcomed several undergraduate and graduate students and these have valued this experience. Everyone in the lab enjoys teaching. Also, I enjoy the inquisitive nature of students that keep challenging our thinking.

3) Current Biosketch:

(please find attached).

4) Trainees over the past 5 years (undergraduate, medical or graduate students; post-doctoral fellows):

- Xin-Bing Han, post-doctoral fellow
- Heather Baskind - Northwestern Undergraduate student - obtained a CMRC summer student Research award in 2006 to work in our laboratory
- Kelly Bergmann - medical student from Midwestern University - obtained a student research award from the Society of Pediatric Research in 2007 to work in our lab. He continues to work as a volunteer twice a week.

Research area (check all that apply):

- Basic Science
- Translational Science
- Clinical Science
- Other _____

BIOGRAPHICAL SKETCH

Provide the following information for the key personnel in the order listed for Form Page 2.
Follow the sample format for each person. **DO NOT EXCEED FOUR PAGES.**

NAME		POSITION TITLE	
DE PLAEN, ISABELLE G		Assistant Professor of Pediatrics	
EDUCATION/TRAINING (Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)			
INSTITUTION AND LOCATION	DEGREE (if applicable)	YEAR(s)	FIELD OF STUDY
Universite Catholique de Louvain School of Medicine, Brussels, Belgium	Candidature en Sciences Medicales	July 1985	Biology
Universite Catholique de Louvain School of Medicine, Brussels, Belgium	M.D.	July 1989	Medicine

A. Positions and Honors.**EMPLOYMENT:**

Residency in Pediatrics, Univ. Catholique de Louvain School of Medicine, Brussels, Belgium	1989-1992
Pediatric Residency, California Pacific Med. Center, Children's Hosp., San Francisco, CA	1992-1994
Residency in Pediatrics, Univ. Catholique de Louvain School of Medicine, Brussels, Belgium	1994-1995
Neonatology fellowship, Children's Memorial Hospital / Northwestern University Chicago, IL	1995-1998
Instructor, Depart. of Pediatrics, Children's Memorial Hospital / Northwestern U. Chicago, IL	1998-2001
Assist. Prof., Depart. of Pediatrics, Children's Memorial Hospital / Northwestern U. Chicago, IL	2001-Present.

HONORS:

1985: Candidatures in Medical Sciences Cum Laude
 1989: MD degree Magna cum laude.
 2005: Excellence in Academic Medicine Award - IDPA- September 2001-August 2003.
 2004: Mentored Clinical Scientist Development Award (K08) – NIH (July 2004-June 2009).
 2005: Excellence in Academic Medicine Award - IDPA- September 2005-August 2007.

PROFESSIONAL SOCIETIES

Endotoxin Society: 1999-present.
 American Academy of Pediatrics (Fellow): 2001-present.
 Society for Pediatric Research: 2004-present.
 American Physiological Society: 2005-present.
 American Gastroenterological association: 2007-present.

PUBLICATIONS**Original research:**

De Plaen IG, Tan X-D, Chang H, Qu X-W, Liu Q-P, Hsueh W: NF- κ B in rat intestine is composed of p50 homodimers and is activated by platelet-activating factor. **Biochim Biophys Acta**, 1392 (1998) 185-192.

2. De Plaen IG, Tan X-D, Chang H, Wang L, Wang L, Remick DG, Hsueh W: Lipopolysaccharide activates Nuclear Factor- κ B in rat intestine: Role of endogenous platelet-activating factor and tumor necrosis factor. **Brit J Pharmacol**, 129 (2000) 307-314.
3. Qu X.-W., Wang H., De Plaen I., Hsueh W. Neuronal nitric oxide synthase regulates the expression of inducible NOS in rat small intestine via modulation of nuclear factor kappa B. **FASEB J**, 15 (2001) 439-446.
4. Chen YH, Lu Y, De Plaen IG, Wang LY and Tan XD: Transcription factor NF- κ B signals anti-apoptotic function of Trefoil Factor 3 on intestinal epithelial cells. **Biochem. Biophys. Res. Commun.** 274 (2000) 576-582.
5. Hummel M, Zhang J, Yan S, **DePlaen I**, Golia P, Thomas G, Varghese T, Li Z, Kaufman DB, Fryer JP, Leventhal J, Stuart FP, and Abecassis MI. Allogenic transplantation induces expression of CMV immediate early genes in vivo. **J of Virology** - 75 (2001) 4114-22.
6. Wang H, Qu X, De Plaen IG and Hsueh W. Platelet-Activating Factor and endotoxin activate CCAAT/enhancer binding protein in rat small intestine. **Brit J Pharmacol** - 133 (2001) 713-21.
7. Rozenfeld RA, Liu X, Deplaen I and Hsueh W. Role of gut flora on intestinal group II phospholipase A2 activity and intestinal injury in shock. **Am J Physiol** - 281 (2001) 281: 957.
9. De Plaen IG, Wang H, Tan X-D, Wang L, Liu Q-P and Hsueh W: Endotoxin, but not platelet-activating factor, activates Nuclear Factor- κ B and increases I κ B α and I κ B β turnover in enterocytes. **Immunology** - 106 (2002) 577-83.
10. Hsueh W, Caplan MS, Qu XW, Tan X-D, De Plaen IG and Gonzalez-Crussi F. Neonatal necrotizing enterocolitis: Clinical considerations and pathogenetic concepts. **Pediatr Dev Pathol** - 6 (2003) 6-23.
11. Han XB, Liu X, Hsueh W and De Plaen IG. Macrophage inflammatory protein-2 mediates the bowel injury induced by platelet-activating factor. **Am J Physiol Gastrointest Liver Physiol.** - 287 (6) (2004): G1220-6.
12. Qu XW, Rozenfeld RA, Chen J, Zhu Y, De Plaen I, Caplan M and Hsueh W. BH4 prevents PAF-induced shock and intestinal necrosis: The role of intestinal nNOS on intestinal perfusion. **Critical Care Medicine** 2005 May;33(5):1050-6.
13. De Plaen IG, Han XB, Liu X, Hsueh W, Ghosh S and May MJ. Lipopolysaccharide induces CXCL2/macrophage-inflammatory protein-2 gene expression in enterocytes via nuclear factor- κ B activation: Independence from endogenous tumor necrosis factor- α and platelet-activating factor **Immunology** 118 (2) (2006) 153-163.
14. De Plaen I.G., Liu SXL, Tian R, Neequaye I., May M., Han XB, Hsueh W, Jilling T, Lu J, Caplan MS. Inhibition of NF- κ B ameliorates bowel injury and prolongs survival in a neonatal rat model of necrotizing enterocolitis. **Pediatric Research** 61(6) (2007) 716-21.

Nonexperimental articles:

1. De Plaen IG and Porta NF: Neonatal diseases of the digestive tract in Pediatrics - just the facts. T. Green, W. Franklin and R.R. Tanz, 113-119- section 24. McGraw-Hill Medical Publishing Division. 2004.

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Principal Investigator/Program Director (Last, first, middle): DE PLAEN, Isabelle G.

2. Hsueh W, Caplan MS, Qu XW, Tan X-D, De Plaen IG, and Gonzalez-Crussi F. Neonatal necrotizing enterocolitis: Clinical considerations and pathogenetic concepts. **Pediatr Dev Pathol** – 6 (2003) 6-23.
3. Hsueh W, Caplan MS, Qu XW, Tan X, DePlaen I, & Gonzalez-Crussi F: Neonatal necrotizing enterocolitis: Clinical considerations and pathogenetic concepts. *Perspectives in Pediatric Pathology, Vol 25: Alimentary Tract Pathology in Infants and Children.* pp. 39-56. Eds: MH Collins, JE Dimmick & DB Singer. 2004.
4. Hsueh W, De Plaen IG, Caplan MS, Qu XW, Tan X-D, and Gonzalez-Crussi F. Neonatal necrotizing enterocolitis: Clinical aspects, experimental models and pathogenesis. **World Journal of Pediatrics** 3 (1) (2007) 17-29.
5. De Plaen IG: Index of suspicion - case 2. **Pediatr Rev** 18(4):137-139, April, 1997.

Grant support:

- Role of Neutrophils in the susceptibility of the neonatal intestine to injury” which has been funded by the Illinois Department of Public Health (September 2001-august 2005).
Awarded– \$ 474,074
- Mentored Clinical Scientist Development Award (K08) entitled: “Mechanisms of acute bowel injury: Role of NF- κ B” – NIH (July 2004-June 2009).
Awarded – 5 years - \$ 625,000
- Children’s Research Foundation (November 2004).
Awarded –\$ 2,500
- “Necrotizing Enterocolitis with Severe injury of the bowel” which has been funded by the Illinois Department of Public Health (September 2005-august 2007).
Awarded– \$ 474,074