BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
MACKMAN, Nigel	John Parker Professor of Medicine
eRA COMMONS USER NAME (credential, e.g., agency login)	
mackman	

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
University of Leicester, England	B.Sc	1981	Biological Science
University of Leicester, England	Ph.D.	1985	Molecular Biology

A. Positions and Honors

Positions and Employment

1984-1987 Postdoctoral Fellow, University of Leicester, England
1987-1989 Research Fellow, Dept. of Immunology, The Scripps Research Institute, La Jolla, CA
1989-1995 Assistant Professor, Dept. of Immunology, The Scripps Research Institute, La Jolla, CA
1995-2002 Associate Professor, Dept. of Immunology, The Scripps Research Institute, La Jolla, CA
2002-2007 Associate Professor with tenure, Depts. of Immunology & Cell Biology, The Scripps Research Institute, La Jolla, CA
2007-present John Parker Distinguished Professor of Medicine, Division of Hematology/Oncology, University of North Carolina, Chapel Hill, NC
2007-present Adjunct Professor, The Scripps, Research Institute, La Jolla, CA

Other Experience and Professional Memberships

1993-1997 Member, Peer Review Committee, California Affiliate, American Heart Association
1995-1997 Member, Thrombosis Study Section, American Heart Association
1997-2002 Member, Pathology A Study Section, NIH
2004-Present Ad Hoc Member, Hemostasis and Thrombosis Study Section, NIH
2005-2007 Member, Peer Review Committee, Western Affiliate, American Heart Association.
2006 Member, NIH/NHLBI Strategic Planning Committee on the Critical Role of Inflammation in Ischemic Disorders
Memberships AHA, ASBMB, NAVBO, ASH and ISTH
Editorial Bds. 2002-2007, *Thromb.Haemost.*
2005-2007, *Arterioscler.Thromb.Vasc.Biol.*
Assoc. Editor. 2007-present, *J.Thromb.Haemost.*
2007-present, *Arterioscler.Thromb.Vasc.Biol.*
2010 Chair, Hemostasis Gordon Research Conference

Honors

1988-1989 American Heart Association, California Affiliate Fellowship
1991 Winner, Louis N. Katz Basic Science Research Prize for Young Investigators, American Heart Association
1995-2000 Established Investigator, American Heart Association
1999 Elected Fellow of the American Heart Association (FAHA)
2004 Special Recognition Award in Thrombosis sponsored by the American Heart Association Council on Arteriosclerosis, Thrombosis and Vascular Biology
2007 Investigator Recognition Award from the International Society for Thrombosis and Hemostasis

B. Selected peer-reviewed publications (of 180 total publications)

1. Yu, L., May, L., Lhotak, V., Shahrzad, S., Shirasawa, S., Weitz, J.I., Coomber, B.L., **Mackman, N.**, Rak, J.W. Oncogenic events regulate tissue factor expression in colorectal cancer cells; implications for tumor progression and angiogenesis. *Blood* 105:1734-41, 2005.

2. Day, S.M., Reeve, J.L., Pedersen, B., Farris, D.M., Myers, D.D., Im, M., Wakefield, T.W., **Mackman, N.**, Fay, W.P. Macrovascular thrombosis is driven by tissue factor derived primarily from the blood vessel wall. *Blood* 105:192-198, 2005.

3. Frank, R.D., Schabbauer, G., Holscher, T., Sato, Y., Tencati, M., Pawlinski, R., **Mackman, N.** The synthetic pentasaccharide, fondaparinux, reduces coagulation, inflammation and neutrophil accumulation in ischemia-reperfusion injury. *J. Thromb. Haemost.* 3:531-40, 2005.

4. Pedersen, B., Holscher, T., Sato, Y., Pawlinski, R., **Mackman, N.** A balance between tissue factor and tissue factor pathway inhibitor is required for embryonic development and hemostasis in adult mice. *Blood* 105:1734-41, 2005.

5. Morrow, D.A., Murphy, S.A., McCabe, C.H., **Mackman, N.**, Wong, H.C., Antman, E.M. Potent inhibition of thrombin with a monoclonal antibody against tissue factor (Sunol-cH36): results of the PROXIMATE-TIMI 27 trial. *Eur. Heart J.* 26:682-8, 2005.

6. **Mackman, N.** Tissue-Specific Hemostasis in Mice. *Arterioscler.Thromb.Vasc.Biol.* 25:2273-81, 2005.

7. **Mackman, N**. Role of tissue factor in hemostasis and thrombosis. *Blood Cells Mol Dis*. 36:104-7, 2006.

8. Tilley, R.E., Pedersen, B., Pawlinski, R., Sato, Y., Erlich, J.H., Shen, Y., Day, S., Huang, Y., Eitzman, D.T., Boisvert, W.A., Curtiss, L.K., Fay, W.P., **Mackman, N**. Atherosclerosis in mice is not affected by a reduction in tissue factor expression. *Arterioscler.Thromb.Vasc.Biol*. 26:555-62. 2006.

9. Rong, Y., Hu, F., Huang, R., **Mackman, N.**, Horowitz, J.M., Jensen, R.L., Durden, D.L., Van Meir, E.G., Brat, D.J. Early growth response gene-1 regulates hypoxia-induced expression of tissue factor in glioblastoma multiforme through hypoxia-inducible factor-1-independent mechanisms. *Cancer Res.* 66:7067-7074, 2006.

10. Schwertz, H., Tolley, N.D., Foulks, J.M., Denis, M.M., Risenmay, B.W., Buerke, M., Tilley, R.E., Rondina, M.T., Harris, E.M., Kraiss, L.W., **Mackman, N.**, Zimmerman, G.A., Weyrich, A.S. Signal-dependent splicing of tissue factor pre-mRNA modulates the thrombogenicity of human platelets. *J.Exp.Med.* 203:2433-40, 2006.

11. Rak, J., Luyendyk, J., **Mackman, N.** Oncogenes, trousseau syndrome, and cancer-related changes in the coagulome of mice and humans. *Cancer Res.* 66:10643-10646, 2006.

12. Frank, R.D., Holscher, T., Schabbauer, G., Tencati, M., Pawlinski, R., Weitz, J.I., **Mackman, N.** A non-anticoagulant synthetic pentasaccharide reduces inflammation in a murine model of kidney ischemia-reperfusion injury. *Thromb.Haemost.*, 96:802-806, 2006.

13. Sevastos, J., Kennedy, S.E., Davis, D.R., Sam, M., Peake, P.W., Charlesworth, J.A., **Mackman, N.**, Erlich, J.H. Tissue factor deficiency and PAR-1 deficiency are protective against renal ischemia reperfusion injury. *Blood* 109:577-583, 2007.

14. **Mackman, N.** Alternatively spliced tissue factor - One cut too many? *Thromb.Haemost.,* 97:5-8, 2007.

15. Redecha, P., Tilley, R., Tencati, M., Salmon, J.E., Kirchhofer, D., **Mackman, N**., Girardi, G. Tissue factor: a link between C5a and neutrophil activation in antiphospholipid antibody-induced fetal injury. *Blood* 110:2433-2441, 2007.

16. **Mackman N**., Tilley R.E., Key N.S. Role of the extrinsic pathway of blood coagulation in hemostasis and thrombosis. *Arterioscler Thromb Vasc Biol.,* 27:1687-93, 2007.

17. Luyendyk, J.P., Piper, J.D., Tencati, M., Reddy, K.V., Holscher, T., Zhang, R., Luchoomun, J., Chen, X., Min, W., Kunsch, C., **Mackman, N**. A novel class of antioxidants inhibit LPS induction of tissue factor by selective inhibition of the activation of ASK1 and MAP kinases. *Arterioscler Thromb Vasc Biol.* 27:1857-1863 2007.

18. Pawlinski, R., Tencati, M., Holscher, T., Pedersen, B., Voet, T., Tilley, R.E., Marynen, P., **Mackman N**. Role of cardiac myocyte tissue factor in heart hemostasis. *J Thromb. Haemost*. 5: 1693-1700, 2007

19. Ghosh, M., Wang, H., Ai, Y., Romeo, E., Luyendyk, J.P., Peters, J.M., **Mackman, N**., Dey, S.K., Hla, T. COX-2 suppresses tissue factor expression via endocannabinoid-directed PPAR δ activation. *J Exp Med* 204:2053-2061 2007.

20. Kerschen, E.J., Fernandez, J.A., Cooley, B.C., Yang, X.V., Sood, R., Mosnier, L.O., Castellino, F.J., **Mackman, N.,** Griffin, J.H., Weiler, H. Endotoxemia and sepsis mortality by non-anticoagulant activated protein C. *J. Exp. Med.* 204: 2439-2448, 2007.

21. Pawlinski, R., Tencati, M., Hampton, C.R., Shishido, T., Bullard, T.A., Casey, L.M., Andrade-Gordon, P., Spring, D., Kotzsch, M., Luther, T., Abe, J., Pohlman, T., Verrier, E.D., Blaxall, B., **Mackman, N.** Role of PAR1 in cardiac remodeling and hypertrophy. *Circulation* 116: 2298-2306, 2007.

22. Milsom, C., Yu, J., May, L., Meehan, B., Magnus, N., Al-Nedawi, K., Weitz, J., Klement, P., Broze, G., **Mackman, N.,** Rak, J. The role of tumor- and host-associated tissue factor pools in oncogene-driven tumor progression. *Thromb. Res.,* 120 Suppl 2:S82-91, 2007.

23. Pawlinski, R., Blaxall, B., **Mackman, N.** Comparison of genetic and pharmacologic approaches to study the role of PAR-1 in cardiac ischemia-reperfusion. *Circulation.* 116: 2298-2306, 2007.

24. Reinhardt, C., von Bruhl, M-L., Masnukyan, D., Grahl, L.,, Lorebz, M., Altmann, B., Dlugai, S., Hess, S., Konrad, I., Orschiedt, L., **Mackman, N.,** Ruddock, L., Massberg, S., Engelmann, S. Protein disulfide isomerase can signal vessel injury for initiation of fibrin generation. *J. Clin. Invest.* 118: 1110-1122, 2008.

25. Tilley, R.E., Holscher, T., Belani, R., Nieva, J., **Mackman, N.** Tissue factor activity is increased in a combined platelet and microparticle sample from cancer patients. Thromb. Res., In press.

26. **Mackman, N.** Tissue-specific hemostasis: role of tissue factor. *J. Thromb. Haemost*. 6:303-305, 2008.

27. Luyendky, J.P., Schabbauer, G.A., Tencati, M., Holscher, T., Pawlinski, R., **Mackman, N.** Genetic analysis of the role of the PI3K-Akt pathway in LPS-induced cytokine and tissue factor gene expression in monocytes/macrophages. *J.Immunol.* 180: 4218-4226, 2008.

28. **Mackman, N.** Thrombosis:triggers, targets and treatments. *Nature*, 451:914-918, 2008.

29. **Mackman, N.,** Moll, S. Venous thromboembolism: a need for more public awareness and research into mechanisms. *Arterioscler.. Thromb. Vasc. Biol.* 28:367-369, 2008.

30. **Mackman, N.** Taubman, M.B. Does tissue factor in vascular smooth muscle cells provide a link between C-reactive protein and cardiovascular disease? *Arterioscler.. Thromb. Vasc. Biol.* 28: 601-603, 2008.

31. Hoffmann, E., Ashouri, J., Wolter, S., Doerrie, A., Dittrich-Breiholtz, O., Scneider, H., Wagner, E.F., Troppmair, J., **Mackman,N.,** Kracht, M. Transcriptional regulation of EGR-1 by the IL-1-JNK-MKK7-c-JUN pathway. *J. Biol Chem* 283: 12120-12128, 2008.

32. Kidd, L, Schabbauer, G.A., Luyendyk, J. P., Holscher, T.D., Tilley, R.E., Tencati, M., **Mackman, N.** *J. Pharmacolo Exp Ther,* In press.

C. Research Support

Ongoing Research Support

R01 HL48872-13 NIH/NHLBI Mackman (PI) 03/01/07 – 02/28/11

Regulation of Inducible Gene Expression in Monocytes

The goals of this project are to study the regulation of tissue factor in monocytic cells exposed to LPS.In addition we will determine the contribution of TF expression by different cell types to LPS induced coagulation in mice.

R01 HL084087-01 NIH/NHLBI Mackman (PI) 09/01/07 – 08/31/11

Role of Par-1 and Par-2 in cardiac remodeling

The goals of this project are to determine the role of Par-1 and Par-2 to inflammation, infarct size, remodeling and hypertophy after myocardial infarction.

University Cancer Research Fund, UNC-Chapel Hill Mackman (PI) 03/01/08- 02/28/09

Chemotherapy and Anti-angiogenic Drug-induced Thrombosis in Cancer

The study will measure levels of TF procoagulant activity in circulating microparticles in cancer patients before and after chemotherapy. Parts of this study overlap with the current proposal.