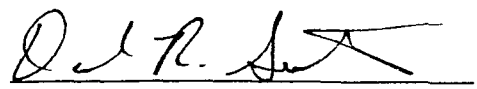
INFLUENCE OF MICROTUBULES ON VASCULAR SMOOTH MUSCLE CONTRACTION

Dahua Zhang

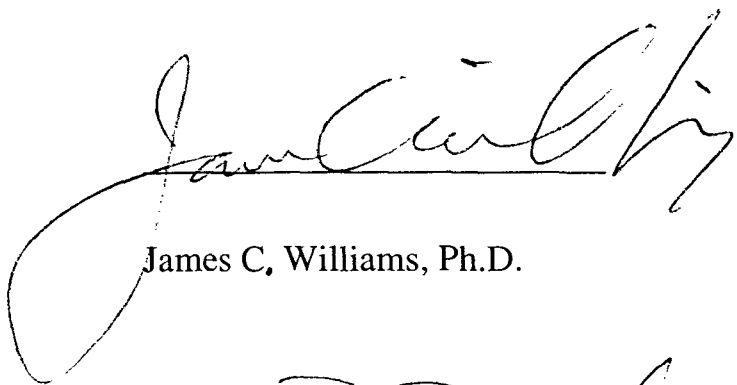
Submitted to the faculty of the University Graduate School
in partial fulfillment of the requirements
for the degree
Doctor of Philosophy
in the Department of Anatomy and Cell Biology, School of Medicine
Indiana University

December 2000

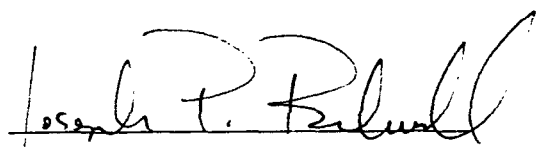
Accepted by the Graduate Faculty, Indiana University, in partial Fulfillment of the requirements of the degree of Doctor of Philosophy



Darl R. Swartz, Ph.D., Chairman

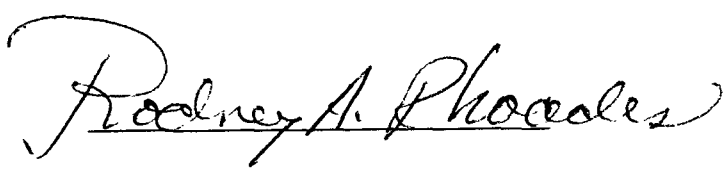


James C. Williams, Ph.D.



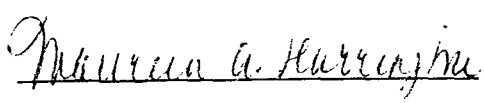
Doctoral Committee

Joseph P. Bidwell, Ph.D.



Rodney A. Rhoades, Ph.D.

Date of Oral Examinatoin
November 6, 2000



Maureen A. Harringon, Ph.D.

Abstract

Vascular diseases, such as hypertension and coronary artery disease, are the leading cause of mortality in the USA and in most Western countries. Investigation of the mechanisms that modulate blood vessel tone is essential for understanding of the etiology and preventing or reducing the complications of these diseases. Vascular smooth muscle is the primary effector in the regulation of blood flow. The regulation of vascular smooth muscle contraction is dependent in part, upon cytoskeleton. Microtubules constitute one of the main cytoskeletal components in eukaryotic cells and play key roles in many cellular activities including mitosis, motility, maintenance of cell shape, intracellular transport, organization of organelles, and signal transduction. However, the distribution of microtubules in vascular smooth muscle and how they are involved in smooth muscle contraction remain unclear. My studies indicate that microtubules run mainly longitudinally in relaxed vascular smooth muscle cells and are compressed instead of depolymerized during contraction. Disruption or stabilization of microtubules does not have a significant effect on shortening velocity of single vascular smooth muscle cells, which suggests that microtubules do not present as an appreciable internal load during smooth muscle cell shortening. Microtubule disruption enhances force production of vascular smooth muscle, and this effect is mediated mainly through modulating Rho/Rho-kinase pathway instead of myosin light chain kinase.

Table of contents