MOLECULAR MOTORS AND ORGANELLE TRANSPORT IN PIGMENT CELLS

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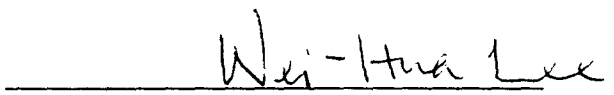
Submitted to the faculty of the University Graduate School
in partial fulfillment of the requirements
for the degree of
Doctor of Philosophy
in Anatomy and Cell Biology
in the school of Medicine,
Indiana University

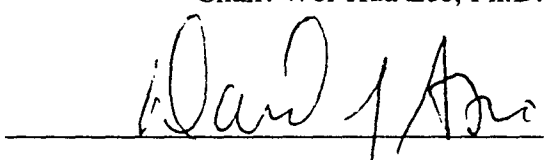
June, 2000

Accepted by the Graduate Faculty, Indiana University, in partial fulfillment of the requirements for the degree of Doctor of Philosophy.

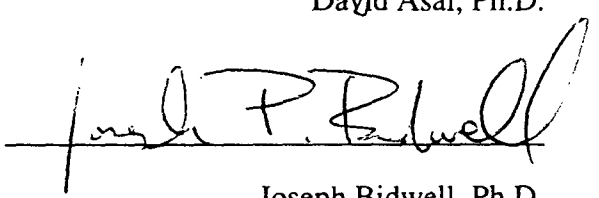
Doctoral Committee:



Chair: Wei-Hua Lee, Ph.D.

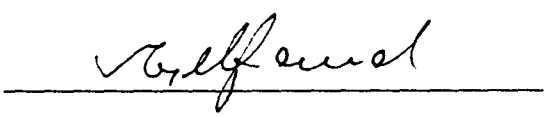


David Asai, Ph.D.

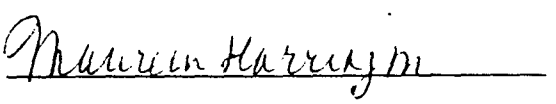


Joseph Bidwell, Ph.D.

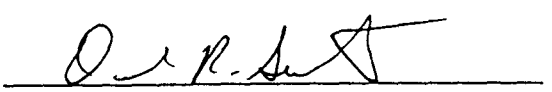
Oral examination on April 28, 2000



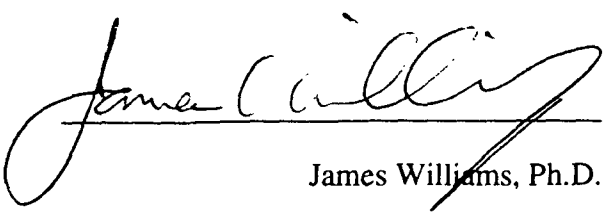
Vladimir Gelfand, Ph.D.



Maureen Harrington, PhD.



Darl Swartz, Ph.D.



James Williams, Ph.D.

Abstract

Melanophores move pigment organelles (melanosomes) from the cell center to the periphery and vice-versa. These bi-directional movements require cytoplasmic microtubules and microfilaments and depend on the function of microtubule motors and a myosin. Here a dominant-negative construct was designed for the study of function of the microtubule motor kinesin II. Kinesin II was shown to be required for pigment dispersion in melanophores, and this was one of the first demonstrations that this motor moves membrane-bound organelles. With the same dominant-negative approach, real-time imaging and single particle tracking analysis were used to determine the contribution of the motors kinesin II and myosin V to pigment dispersion. In cells with inhibited kinesin II melanosomes lack fast saltations and move slowly in random directions, never reaching the periphery of the cell, while in cells lacking active myosin V, melanosomes saltate rapidly but do not remain at the cell periphery. The observation that in double mutants there is no movement of melanosomes indicates that kinesin II and myosin V are the only motors required for dispersion. The work presented here led to the following conclusions: 1, pigment dispersion has two components, a fast and a slow one; 2, kinesin II is responsible for the fast component and myosin V for the slow component of dispersion; 3, myosin V modulates the action of microtubule motors. The data presented here demonstrate that a functional cooperation occurs between kinesin II and myosin V and that motor interaction *in vivo* has regulatory implications to net organelle movement. These results have widespread implications for organelle transport and motor interaction in other systems.

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