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18 November 1996

Dr. Philip J. Migliore
Chairman and Research Director
Scientific Advisory Committee of The Moran Foundation
Department of Pathology
Baylor College of Medicine
Texas Medical Center
Houston, TX 77030

Dear Dr. Migliore,

Enclosed please find the annual progress report for funding received during 1996 from the Moran Foundation for a project entitled "An Animal Model System to Study Eye Development" (project number 1-95-0081).

Funding from the Moran Foundation is an important mechanism for initiating new research efforts and is greatly appreciated.

Sincerely,

Graeme Mardon, Ph.D.
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Annual Progress Report for Moran Foundation Funded Work

Principal Investigator: Graeme Mardon, Ph.D.

Project Title: **An Animal Model System to Study Eye Development**

Project Year: **1996**

Project Number: **1-95-0081**

Summary of Progress

The overall goal of our original proposal was to look for DNA-binding activity of the novel nuclear protein encoded by the *Drosophila* gene *dachshund*. Our approach was two-fold: First, we looked for evidence of DNA-binding activity of the Dachshund protein. Then, we proposed to look for specific DNA sequences that could be bound by Dachshund protein.

We have made excellent progress on the first phase of this project and are just now beginning work on the second phase. Initially, we proposed to conduct DNA binding studies using either in vitro translated Dachshund protein or extracts of cell lines expressing recombinant Dachshund protein. However, we decided to take a slightly different approach to this first step. Instead of looking for evidence of DNA-binding in vitro, we looked in vivo. Specifically, we expressed Dachshund protein in the larval salivary glands using a transgene combining a heat-shock promoter with a *dachshund* cDNA. Chromosomes in the salivary gland of *Drosophila* larvae are polytene; that is, they are present in up to 1000 copies per cell and are all paired together forming large and easily visible chromosomes with distinct banding patterns. After expressing Dachshund protein in the salivary gland with a heat shock pulse, we prepared chromosome "squashes" where the chromosomes are laid out on a slide and are available for immunohistochemistry. Using our monoclonal antibodies prepared against the *Drosophila* Dachshund protein, we were able to visualize specific staining on a subset of chromosomal bands. These results provide preliminary evidence that the Dachshund protein is able to associate with DNA or chromatin in vivo. Moreover, since the protein was detected at specific positions along the chromosomes, it seems likely that Dachshund protein associates with DNA in a site-specific manner. In addition, we also know what sites in the genome are bound by Dachshund protein because of the unique banding pattern of the polytene chromosomes. However, whether the Dachshund protein hinds directly to DNA or via other DNA-binding proteins is not known.

Now that we have good preliminary evidence that the Dachshund protein may be able to bind DNA, we will move forward with the other experiments outlined in our proposal designed to look for non-specific and specific DNA-binding activity by Dachshund protein in vitro.