ipif
Incontinentia Pigmenti International Foundation

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LETTER FROM THE EXECUTIVE DIRECTOR

In keeping with my previous assumptions that those who read this newsletter are most interested in learning the latest news in the field of research of IP, I have asked David Nelson, Ph.D., of Baylor College of Medicine (a leading researcher in the IP International Research Consortium) to write an article on the current work being done in research, now that the gene has been identified. His laboratory assistant at the time the Nemo gene was identified has left the laboratory and Dr. Christine Shaw has taken his place. Dr. Nelson has written a short biography of Dr. Shaw which I think you will find interesting.

I also have requested Ashley Badgwell, MS to do an update on the Natural History Project that was started in 2003. Ms. Badgwell, who conducted the survey and compiled the results, has now done an update. This is a project which will continue for many years to come and we will report updates on current findings periodically in this newsletter.

I was delighted that IPIF was the recipient of some very imaginative fundraising projects. I've asked those whose events these were to write stories about them. It is hard to describe how very grateful IPIF is for the time and effort that went into making sure that these undertakings were successful.

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IP NATURAL HISTORY UPDATE

Ashley Badgwell, MS and
Judith Willner, MD
Mount Sinai School of Medicine

Last spring, a summary of the Incontinentia Pigmenti Natural History Study was published in this newsletter. For those of you unfamiliar with the project, Dr. Willner, Director of Clinical Genetics at Mount Sinai School of Medicine and I, then a graduate student at Mount Sinai in New York City, saw the need for an IP natural history analysis based on physician and patient reports. A questionnaire was developed to assess the affected individual's experience with IP. It was sent to IPIF members, with the help of Susanne Emmerich and made available on the website. As of March 2003, 152 completed surveys were returned and included in our initial analysis. Since that time, we have received 42 additional completed surveys, bringing the total number of participants to 194. Again, we are very grateful to those who participated. In this article, we present an update of the data along with a discussion of interesting findings.

First, a review of the statistical tools employed in the analysis may help readers to better understand the data and appreciate the importance of sample size. We understand that the 194 people included in this study represent only a fraction of the worldwide population with IP. Of course, as the number of participants increase, our understanding of IP becomes more accurate. Because of the nature of our data, we decided to use 95% "confidence intervals" to determine the statistical significance of the findings. The definition of confidence interval is "the range within which the true magnitude of effect lies within a certain degree of assurance". In this study, you will find the confidence interval as two numbers in parentheses, following a frequency or average. For example, when you read that 49% (45%,53%) of the participants in this study have misshapen nails, that means that we expect that the true percentage

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RESEARCH UPDATE

David L. Nelson, Ph.D.
Baylor College of Medicine

Research is progressing in a number of areas to understand the causes and consequences of Incontinentia Pigmenti. These areas can be divided into characterization of the NEMO protein's normal functions, determining the consequences of its absence in model systems, and understanding the various mutation types and how they exert their effects.

Several laboratories have been working to describe the role of NEMO in cells and tissues. Among the most interesting findings have come from the realization that NEMO plays a role in cells' responses to DNA damage. These studies have helped to define parts of the protein that participate in these responses, how they respond through modification, and to better understand the impact of mutations in these regions.

One of the most useful tools available to geneticists is the laboratory mouse, which can be manipulated to carry mutations similar to those found in human diseases. Several models of Incontinentia Pigmenti have been described, and these continue to be studied. Unfortunately, these do not model the disease particularly well, since female mice appear to clear the mutant cells more effectively than human females. To get around this problem, groups are in the process of making mice in which the mutation can be introduced later in development and/or in specific tissues. These should allow better definition of the effects of the IP mutation in various tissues.

Finally, new families with unusual mutations, in addition to those with the common deletion mutation, continue to come to the attention of researchers. These mutations help to define the parts of the NEMO protein that are important for function. In addition, more mutations that lead to the ectodermal dysplasia and immune deficiency disorder have been defined. Again, these help researchers to understand the role of different parts of

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