

THE GENE CAUSING INCONTINENTIA PIGMENTI HAS BEEN IDENTIFIED

An event has occurred that many of us have been dreaming about. The gene which causes IP has been identified. I would like to tell the story of how this remarkable achievement came about. (continued on page 2 col. 1)

LETTER FROM THE EXECUTIVE DIRECTOR

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CELEBRATION DINNER

Members of the International IP Research Consortium

(Clockwise from left to right) Asmae Smahi, Susanne Emmerich, Alfredo Ciccodicola, Nina S. Heiss, Swaroop Aradhya, Sue J. Kenwrick, Richard A. Lewis, Hayley Woffendin, Annemarie Pouska, Michele D'Urso, Teresa Esposito, David L. Nelson, Tracy Jakins.

In December of 1999, the International IP Research Consortium met at the Hilton Hotel at Gatwick Airport in London, England. It was shortly after everyone realized that a mutation on the NEMO gene was definitely the cause of IP. The meeting began on Saturday morning and lasted all day. During this period, all the facts were reviewed and discussed. When it was dinner time, a large table had been set aside for the group in the dining room and the celebration began.

once again and the results were conclusive.

The excitement that overtook everyone is very hard to describe. It was the end of a very long and difficult journey.

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LETTER

In the Fall of 1994, a baby girl covered with blisters was born into my extended family. She was misdiagnosed as having an infectious disease, treated aggressively with incorrect medication and was looked after by parents who were emotionally devastated. It took 4 more months to get a correct diagnosis. Finding accurate information was extremely difficult, finding a support group impossible. I made a promise to the baby that when she was old enough to have her own children, the mysteries of IP will have been uncovered, and she would not have to suffer the experience of her parents.

I began by creating the National Incontinentia Pigmenti Foundation, Inc. With the identification of the gene, half of my promise has been realized. It would not have been possible for one person working alone to accomplish the goals that I set for the Foundation. I would therefore like to acknowledge all those who helped me make this promise come true. To simply say thank you is hopelessly inadequate. The lives of so many people will be profoundly altered by this discovery.

I will begin with the International IP Research Consortium (IIPRC), which I organized in 1996. A list of the members with their photographs appears on page 3. This group of truly remarkable people worked together in a unique collaboration. Many consortiums have existed, only to fall apart through competitiveness, lack of cooperation and petty antagonisms. But the IIPRC is outstanding in several ways. Its members are a group from differing backgrounds, nationalities (7) and disciplines who have bridged the multiple geographic, language, and intellectual barriers to work on one focused problem: the genetic nature and cause of IP. They question each other respectfully, each accepting the challenge of his or her work assignment with equanimity and humor. For years

the IIPRC met over a weekend every six months, many traveling thousands of miles. In between meetings there was always a flurry of e-mails sharing information, theories, results, etc. Many dead-end paths were encountered along the way, disappointing results taken in stride, theories that didn't pan out, etc. Through all this not one person ever thought or spoke of giving up. All those who benefit from their extraordinary efforts and eventual success can never know the full extent of their dedication. The second group, which is vital to this effort, are those who participated in the research. The adults with IP, parents, children and extended family members who agreed to share clinical information and send samples of their blood to the consortium lab nearest them, were invaluable. No research could have gone forward without the ability to examine and study this group. Another vital component is donations. How do we express adequately our gratitude to those who have contributed financially or who have assisted in raising funds, thereby having made the above achievements possible? The Foundation funds its own expenses which are becoming considerable, even though no salaries or rents are paid. There are the costs of telephone, printing, postage, etc. The Foundation funds researchers in England, France and the clinical department of the research lab in Texas. It also pays for many of the expenses of the Consortium meetings which historically have taken place every six months, but which now occur more frequently.

It is important to remember that this is only Step One. The isolation and cloning of the gene for Incontinentia Pigmenti is a substantial achievement, but it is only the beginning of our understanding the impact on molecular genetics, molecular and developmental biology, embryology, and the realistic investment in the understanding of its roles in brain (retardation and seizures), vision (retinal vascular development and retinal detachment), skin (eruptions and

scarring), teeth (formation and enamel development), and immunology (eosinophilia).

There are those who must be thanked who do not fall into the above groups. Families, Scientific Advisory Council members of NIPF, friends and countless others who play a continuing and vital role.

We will all continue to work together until we reach our final goal. And once again, I thank you all for helping me to keep my promise.

Susanne Bross Emmertich

**NATURE MAGAZINE
May 25, 2000
"A RECURRENT GENOMIC
REARRANGEMENT IN
DEFECTIVE NF KAPPA B
(NF-KB) ACTIVATION, IS
THE MOST COMMON
CAUSE OF INCONTINENTIA
PIGMENTI (IP)."**

The article in Nature Magazine is 7 pages long and is very technical. I have therefore decided that instead of reproducing the article in its entirety, it would be preferable to reprint just the abstract and acknowledgments. For those who wish the whole article it can be obtained by writing to NIPF at the address listed on the cover page.

Abstract

Familial Incontinentia Pigmenti (IP) is a neurocutaneous genodermatosis that segregates as an X-linked dominant disorder with a high probability of prenatal male lethality. Among surviving affected females, its prominent phenotypic manifestations include abnormalities of the skin, hair, nails, teeth, eyes and the central nervous system. Patients exhibit early inflammatory skin lesions and cells expressing the mutated X are selectively eliminated. The locus for the disorder has been linked genetically to the (continued on page 4 col. 1)

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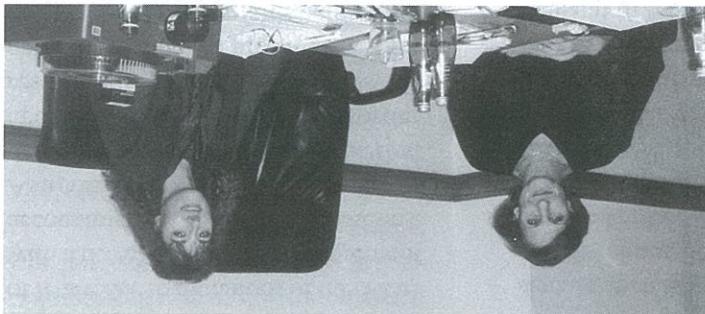
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