

to finding a cure. I urge my colleagues to take the time to read this article and learn more about this terrible disease.

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GENETIC BREAKTHROUGHS TAKE CENTER STAGE IN ACCELERATING POLYCYSTIC KIDNEY DISEASE DRAMA

(By Michael D. O'Neill)

INTRODUCTION

"I believe the future holds the prospect of fundamental breakthroughs that will allow us to develop treatments that will change the basic biology of polycystic kidney disease (PKD)."

This hopeful message was delivered by Josephine Briggs, MD, director of the Division of Kidney, Urologic, and Hematologic Diseases in the National Institutes of Health's National Institute of Diabetes and Digestive and Kidney Disease (NIDDK), in her luncheon address at the 8th Annual Conference on PKD, sponsored by the Polycystic Kidney Research (PKR) Foundation, in Nashville, TN.

In 1982, Joseph H. Bruening and Jared J. Grantham, MD, founded the PKR Foundation to determine the cause, improve clinical treatment, and discover a cure for PKD. Today, the organization is the major funder of private PKD research grants and the disseminators of information about the disease worldwide to physicians, researchers, patients, and the general public.

Briggs' optimism was based on a continuing series of dramatic discoveries related to the genetics and molecular biology of PKD. These discoveries have come at an ever-increasing pace following identification of the PKD1 and PKD2 genes in 1994-1995 and 1996, respectively, and have roughly paralleled an increasing rate of PKD-directed research funding by both the NIH and the PKR Foundation.

ADDITIONAL ADVANCES

Additional advances in the last few months have generated even more excitement. Gregory Germino, MD, a nephrologist at The Johns Hopkins University School of Medicine, Baltimore, MD, has shown evidence that a two-hit mechanism initiates cyst formation in PKD and suggested that intervention to prevent the second hit may impact the course of the disease.

Germino has shown that the normal PKD1 and PKD2 proteins physically interact with each other in the cell membrane and probably participate in a common cellular pathway. This finding may explain why defects in either of these genes, located on different chromosomes, can cause the same clinical disease.

Briggs termed these discoveries "enormous, dramatic, and, in some cases, very surprising." She said that "have implications not only for PKD, but perhaps for other diseases as well."

Germino described his findings at one of the conference's many informative workshop sessions. Attendees also heard encouraging news about the prognosis for children with autosomal recessive PKD (ARPKD), and prenatal diagnosis of ARPKD. They also received updates on numerous other areas of PKD research and treatment.

In her address, Briggs also commented on the future of funding for PKD research and stressed the need for industry involvement on the parts of both the biotech and pharmaceutical industries.

PKD BACKGROUND

PKD is a systemic disease. The most common problems are associated with the kidneys, where fluid-filled cysts can develop and lead to End-Stage Renal Disease (ESRD). As

with other forms of ESRD, dialysis and transplantation are the available treatments.

There are two major forms of PKD—the more common, autosomal dominant (ADPKD) form that chiefly affects adults, and the much rarer autosomal recessive (ARPKD) form that affects children.

ADPKD affects an estimated 600,000 people in the U.S. and 12.5 million around the world. It is said to be the most common life-threatening genetic disease.

In the US, over 1,000 people die each year from PKD, and an additional 2,000 develop kidney-failure. Costs to US taxpayers from dialysis, transplants, and treatment related to this disease are estimated at more than \$1 billion annually.

Defects in the PKD1 gene on chromosome 16 are responsible for 85% of ADPKD while defects in the PKD2 gene on chromosome 4 are responsible for about 15%. A third gene (PKD3), which has not yet been pinpointed, is defective in a small number of ADPKD families. The gene for ARPKD has not yet been identified, but it has been located within a small region of chromosome 6.

THE TWO-HIT MECHANISM

ADPKD patients are born with one defective PKD gene and one functional PKD gene. For PKD1-associated ADPKD, Germino has shown compelling evidence that cysts develop from a subset of kidney cells in which both PKD1 genes are defective.

Germino describes this as a two-hit mechanism. The first hit is being born with one broken PKD1 gene. The second hit is sustaining damage to the remaining functional PKD1 gene. This second hit leaves the cell with no way to produce the normal PKD1 protein, and that deficiency somehow leads to cyst formation.

This two-hit model is particularly attractive because it offers an explanation for two-fundamental puzzles of PKD, namely the highly variable course of the disease and the focal nature of cyst formation (in PKD, only one out of every 100 or 1,000 nephron tubule cells actually goes on to become a cyst—the vast majority of these cells are completely normal).

This argument proposes that the cysts develop only from those cells that experience second hits and that the variable disease course might be traceable to variable frequencies of the second hits in different individuals.

CELL MEMBRANE INTERACTION

The second dramatic finding, reported in the June 1997 issue of *Nature Genetics*, is that the normal PKD1 and PKD2 proteins interact in the cell membrane and probably work together in a common cellular pathway. As noted earlier, this finding may explain why defects in either of these genes can cause the same clinical disease.

"By understanding pieces of this cellular pathway and the steps involved, we hope that we can one day design safe and effective therapies for PKD," Germino said.

HOPE FOR ARPKD PATIENTS

Encouraging news concerning ARPKD was reported by Lisa Guay-Woodford, MD, a pediatrician and assistant professor of Medicine at the University of Alabama-Birmingham.

"Still, in 1997, there is a sense among the general medical community that ARPKD is a universally fatal disease," she remarked. "The answer is that it is not. While it's true that 30%-50% of these children will not survive the newborn period, results from two recent studies have shown that, if a child with ARPKD can survive the first year of life, that child has a reasonably good prognosis."

Guay-Woodford said that, if sufficient family information is available, it's possible to

carry out prenatal diagnosis for this disease, using DNA-based genetic linkage analysis. With collaborators, Guay-Woodford has performed such diagnoses in a number of cases where the fetus was known to be at risk for ARPKD.

NIH AND PKD FUNDING

In her luncheon address, Briggs stressed the urgent need for the biotech and pharmaceutical industries to become more involved in the funding of PKD research. She noted that the estimated cost of taking a single drug to market is \$270 million, which exceeds the entire NIH budget for kidney disease research.

"If we are going to eventually see new drugs for PKD, we also need pharmaceutical and biotech investment," she said.

While noting that NIH funding for PKD research had increased significantly—from \$70,000 (one grant) in 1982 to \$7.3 million (46 grants) in 1996, Briggs, a nephrologist and kidney researcher, expressed her desire for increased NIH funding in the area of PKD research. The PKR Foundation has previously stated that annual NIH funding for PKD research has trailed allocations for diseases that affect fewer people. Cystic fibrosis, for example affects 30,000 people in the US and received \$61 million in annual funding from the NIH in 1996 while PKD affects 600,000 and received only \$7.3 million.

In 1996, the PKR Foundation funded \$536,000 in PKD research and will fund \$750,000 by the end of this year.

"We directly fund individual investigators at major teaching and research institutions and heavily promote the need for increased PKD investigation at the federal level," according to Dan Larson, PKR Foundation president. "We plan to work closely with Dr. Briggs and the appropriations committees to add a zero to the current PKD research allocation of \$7.3 million."

GIVE THEM AN ADULT WHO CARES

HON. DONALD M. PAYNE

OF NEW JERSEY

IN THE HOUSE OF REPRESENTATIVES

Monday, June 22, 1998

Mr. PAYNE. Mr. Speaker, as youngsters we're taught about pride and humility and how we must use them if we are to serve well and succeed in life. Today, proud and humble, I would like to join others as they honor and recognize my brother, William, for his work as a New Jersey State Assemblyman representing the 29th Legislative District. Tomorrow at an event at the prestigious law firm of Gibbons, DelDeo, Dolan, Griffinger & Vecchione in Newark, New Jersey, family, friends, colleagues and supporters will gather to thank and further encourage Assemblyman Payne on the leadership he has continuously exhibited to benefit the lives of those less fortunate among us.

Assemblyman Payne is serving his first term where he is a member of the powerful Appropriations Committee. My brother, Bill, is no stranger to the political process. He was the first African American elected as District Leader in Newark's North Ward in 1955. He unsuccessfully sought municipal elected office in 1962 when he lost by 399 votes a run-off election for Councilman-at-Large. He ran a spirited race for South Ward Councilman in 1966 which was also unsuccessful. Over the years he has assisted numerous citizens in their

quest for elected office. He was among the first to encourage Kenneth A. Gibson, Newark's first African American Mayor, to actively seek political office. And, of course, I am another of his proteges. Since taking the oath of office this year in January, Assemblyman Payne has energized the New Jersey Legislative Black and Latino Caucus.

I would like to bring my colleagues attention to two pieces of legislation Assemblyman Payne has introduced—a bill establishing a 21-member Amistad Commission to develop education and public awareness programs about the history of slavery in America and the post-slavery triumphs of African Americans.

He has also introduced a bill that would require all the New Jersey's school districts to have a program that links troubled children with volunteers who promise to spend at least one hour a week with them for at least one year. Prior to his election, Assemblyman Payne has actively recruited hundreds of mentors to work with some of our troubled youth. These mentors occupations ranged from doctors and lawyers to retirees and laborers—people who knew the importance of being a caring adult in the lives of sometimes confused and troubled youngsters. Assemblyman Payne was himself a mentor to a young man who was destined to get into trouble. Today, Rahjan Williams, the mentee, is looking forward to attending college to become an accountant.

Mr. Speaker, I am sure my colleagues will join me as I extend congratulations and best wishes to my only brother of whom I am extremely proud. And I wish to thank those who are honoring him, especially his son-in-law Wilfredo Benitez, an up and coming young attorney with the host law firm

“KUDZU” CONCLUDES
SUCCESSFUL WASHINGTON RUN

HON. DAVID E. PRICE

OF NORTH CAROLINA

IN THE HOUSE OF REPRESENTATIVES

Monday, June 22, 1998

Mr. PRICE of North Carolina. Mr. Speaker, I would like to recognize the artistic merit and creative talents of North Carolinians Doug Marlette, Jack Herrick, and Bland Simpson, creators of “Kudzu: A Southern Musical.” This musical production has been playing at the Ford's Theatre in Washington, DC for almost sixteen weeks, has received glowing reviews from the New York Times, the Boston Globe, and other publications, and has lifted the spirits of thousands who have been privileged, as I was last week, to see the show.

The musical is based on the syndicated comic strip “Kudzu,” illustrated by Pulitzer Prize-winning editorial cartoonist Doug Marlette. The Red Clay Ramblers, a talented and versatile musical group from Chapel Hill, are featured along with an excellent cast. The production explores life in a small Southern town called Bypass and focuses on the life, loves, and mishaps of a character named Kudzu (which is also the name of the incredible vine that has engulfed half the town but hides wondrous treasures beneath).

Having grown up in a small Southern town myself, I could easily identify with their portrayal of the South and instantly recognize many of the characters! However, you do not

have to be Southern, or even follow the antics of Kudzu, Rev. Will B. Dunn, and the other Bypass regulars in the comics, to enjoy this family show. Doug Marlette, Jack Herrick and Bland Simpson wrote a clever and entertaining script and incorporated great bluegrass and Dixieland music to make this production enjoyable for all audiences. It's as funny as can be, but it also tugs at the heartstrings and reminds us of the things that matter most in life.

I commend this North Carolina trio, the cast of “Kudzu,” and director Lisa Portes for their tremendous work in making this production such a success. They tell a great story and I am proud that they call North Carolina home.

HONORING TERRI THOMSON

HON. GARY L. ACKERMAN

OF NEW YORK

IN THE HOUSE OF REPRESENTATIVES

Monday, June 22, 1998

Mr. ACKERMAN. Mr. Speaker, I rise today to honor and congratulate Terri Thomson, on her swearing in as the Queens member of the New York City Board of Education. She is a dynamic and energetic individual, who will work tirelessly on behalf of the thousands of students in the New York City Public School System. Terri began working as a staff assistant in my Queens office when I served in the New York State Senate. I quickly became impressed with her work ethic, and her political savvy. Shortly after being elected to Congress in 1983, I promoted her to be my district administrator where she served with the utmost integrity and compassion until 1990. In this capacity, she made a difference in the lives of thousands of my constituents. Aside from being an invaluable political ally, she became the dearest of friends both to me and to my family.

After leaving my office, she was hired by Citibank as the Director of Community Relations and was eventually promoted to be the Vice President of City and State Governmental Relations. At Citibank she helped school principals with professional training and worked to integrate new technology into the public school system. Moreover, she was able to introduce students to the Internet and demonstrated its application to commercial banking.

Throughout her career, Terri has been deeply involved in the community. She also serves as the Vice Chair of the Brooklyn Sports Foundation, which seeks to create an indoor sports facility for the New York City Public School System. Terri has also been involved with the Queens Chamber of Commerce and the Queens Public Library where she sought to improve both economic and educational opportunities for the entire community.

Terri's commitment to the community, her understanding of the issues, and her public and private sector experience make her uniquely qualified for a position on the New York City Board of Education. I am fully confident that she will be thoroughly equipped to grapple with the enormous complexities of the New York City Public School System. Thus, I ask all of my colleagues in the House of Representatives to join me in honoring this extraordinary individual whose dedication to the community will continue to make a significant

difference in the lives of thousands of New Yorkers.

PERSONAL EXPLANATION

HON. GIL GUTKNECHT

OF MINNESOTA

IN THE HOUSE OF REPRESENTATIVES

Monday, June 22, 1998

Mr. GUTKNECHT. Mr. Speaker, last Thursday and Friday, June 18 and 19, due to my son's graduation, I missed roll call votes 245 and 251. Had I been present I would have voted as follows:

On roll call vote number 245, on establishing the Select Committee on U.S. National Security and Military/Commercial Concerns With the People's Republic of China, yea.

On roll call vote number 246, on ordering the previous question on the resolution establishing the rule for further consideration of H.R. 2183, yea.

On roll call vote number 247, on agreeing to the resolution establishing the rule for further consideration of H.R. 2183, yea.

On roll call vote number 248, on agreeing to the resolution establishing an open rule for consideration of H.R. 4059, the military construction appropriations bill, yea.

On roll call vote number 249, on agreeing to the Thomas amendment to the Shays substitute to H.R. 2183, the Bipartisan Campaign Integrity Act, yea.

On roll call vote number 250, on agreeing to the Maloney amendment to the Shays substitute to H.R. 2183, the Bipartisan Campaign Integrity Act, yea.

On roll call vote number 251, on agreeing to the Gillmor amendment to the Shays substitute to H.R. 2183, the Bipartisan Campaign Integrity Act, yea.

U.S. IMMIGRATION COURT

HON. BILL MCCOLLUM

OF FLORIDA

IN THE HOUSE OF REPRESENTATIVES

Monday, June 22, 1998

Mr. MCCOLLUM. Mr. Speaker, today I am introducing legislation to establish a new United States Immigration Court. The title of the bill is the “United States Immigration Court Act of 1998.” This bill would remove the immigration adjudication functions from the Justice Department and invest them in a new Article I court. The court would be composed of a trial division and an appellate division whose decisions would be appealable to the Court of Appeals for the Federal Circuit.

The system for adjudicating immigration matters has matured tremendously over the last 15 years. Special inquiry judges have become true immigration judges. The Board of Immigration Appeals has been greatly expanded, and the whole Executive Office for Immigration Review has been separated from the Immigration and Naturalization Service.

Yet much of this system, including the Board of Immigration Appeals, does not exist in statute. And while separated from the INS, aliens still take their cases before judges who are employed by the same department as the trial attorneys who are prosecuting them.

It is time to take the next logical step and create a comprehensive adjudicatory system