

## The National Cell Repository

is a repository for families with Alzheimer Disease or severe memory loss. Families having two or more living individuals with memory loss are encouraged to participate. We would like to thank the hundreds of families nationwide who are already participating in the National Cell Repository. Many family members have provided blood samples, which researchers use to study Alzheimer disease (AD) and other related diseases. Our hope is that, through the efforts of our participants, we will one day unravel the mystery of devastating diseases, like AD. We are always eager to accept new families to help us move toward this goal.

### National Cell Repository for Alzheimer's Disease Department of Medical Genetics

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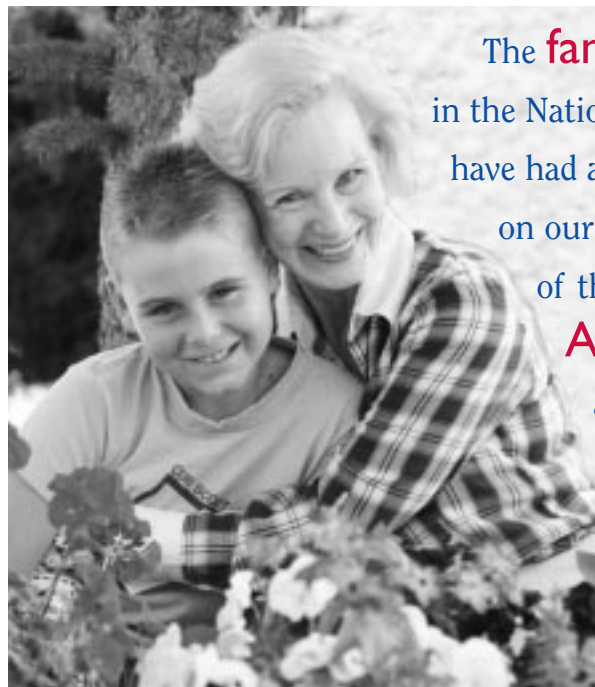
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# NCR Update

Newsletter of the National Cell Repository for Alzheimer's Disease Volume 2 ■ October 2002



The **families** participating in the National Cell Repository have had a **great impact** on our **understanding** of the genetics of **Alzheimer** disease and dementia.

## A Decade of Research Using the National Cell Repository

Tatiana Foroud, Ph.D.

**T**he National Cell Repository was established in 1991 to collect and maintain clinical information and DNA samples on large numbers of families having multiple individuals affected with Alzheimer disease.

For over a decade, family history information and samples have been provided, in a non-identifiable fashion, to researchers interested in studying the genetics of AD and related diseases. Nearly 50 different AD scientists have used samples from the National Cell Repository in their research studies. This has resulted in nearly 60 scientific publications. These publications have been helpful in providing a better understanding of the genetics of AD. A very important finding that resulted from the use of these samples was the confirmation that the Apolipoprotein E4 allele increases the risk for AD.

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# Financial Planning: Paying for Long Term Care

For many older adults, the high cost of long-term care presents one of the greatest threats to financial security. Medicare does not cover long stays in a nursing home and home health care coverage is very limited. The vast majority of Medicare supplement (“Medigap”) policies offer little or no long-term care coverage. In fact, less than 5% of the costs of nursing home care in this country are paid by either Medicare or private insurance. Most families pay these costs out of their savings until they reach poverty level and then turn to the Medicaid program for assistance. This is particularly tragic when a couple is involved and the spouse of the nursing home resident is left in poverty. Planning ahead can help alleviate these harsh results.

## LONG TERM CARE INSURANCE

In response to the financial jeopardy faced by most older adults, many insurance companies have begun offering long term care insurance or “nursing home policies.” In the past five years, product descriptions and features have changed dramatically. Choosing this type of policy requires special caution. The following questions may be helpful as you evaluate a policy:

### Will the policy deliver benefits when you expect it to?

Most people in nursing facilities are not there for treatment of a medical problem; they are there because they need supervision or assistance with activities of daily living. However, many long term care insurance policies require that the care be “medically necessary.” The definition of that term in the insurance contract is very important. Many policies limit coverage to “skilled care” and do not cover the more common intermediate level or custodial care. Others limit coverage to circumstances when Medicare pays or to Medicare approved facilities. Furthermore, “skilled care” can be defined differently between policies, and often is very different from the Medicare definition.

### Can you be dropped from, or priced out of, this policy?

Renewability is critical. A policy that can be cancelled by the company after a need arises may be worthless. Also look for provisions that control increases in premiums. A number of insurance companies were prosecuted in 1999 for illegally raising premiums on policies that were advertised to have “fixed premiums”.

### Will the policy’s benefits cover your needs?

Carefully evaluate maximum benefit levels as well. Since the individual purchasing such insurance is looking for

long term protection, coverage at the rate of \$75 per day may seem very good now, but may be totally inadequate to cover inflated prices by the time the person requires nursing home care. Pre-existing condition clauses must also be carefully reviewed. Be very wary of an insurance salesman who encourages you to omit mention of existing or previously diagnosed conditions, since the company may not later be bound by an overzealous salesman’s representations to you.

The long term care insurance buyer should shop carefully and seek expert assistance in analyzing long term care insurance policies.

## MEDICAID ELIGIBILITY CONSIDERATIONS

The Medicaid program, originally designed as a safety net program for the poorest people, now finances nursing home care for many nursing home residents. Thus, the program now has a major impact on the financing of long term health care. It is only sensible to have a basic knowledge of the help available through the Medicaid program. This knowledge, combined with expert advice, can help preserve family assets while qualifying for Medicaid assistance.

There are three primary issues that may determine Medicaid eligibility: Assets, Income, and Transfers of Assets.

### Assets

The amount of assets that can be kept by Medicaid recipients and their families depends on whether or not the applicant is married, and if so, whether the applicant’s spouse is still living in the community.

Assets that are counted include cash and all assets that can be converted to cash such as CDs, stocks, bonds, other investments (including those in tax-qualified plans such as IRAs), life insurance that has a cash surrender value, real estate other than the home, and other assets.

You should note that not all assets are counted when determining the maximum asset limits that may be retained by the applicant and/or the community spouse.

### Income

Generally, all of the income of Medicaid recipients must be paid toward the cost of their medical care, and then Medicaid covers any remaining costs. Each recipient,

however, is allowed to keep \$50 each month for personal use. The Medicaid rules do not require that the income of the community spouse be spent on the Medicaid recipient's care. Also, if the community spouse has a low monthly income, it is possible for the community spouse to get an allowance from the income of the Medicaid recipient spouse.

### Transfers of Assets

There can be a period of Medicaid ineligibility for applicants and their spouses who have transferred assets without receiving full value for the assets within the last 3 years [5 years for certain transfers into trusts]. This is a highly technical rule and must be analyzed very carefully in any estate planning involving gifts, for the time and amount of the gift can cause unexpected results.

### Medicaid's Spousal Impoverishment Rules

There is a special provision of federal law that allows a community spouse with a low income to seek to keep a greater portion than just half the assets, in order to generate enough income to meet the community spouse's Minimum Monthly Maintenance Needs Allowance. This procedure involves the appeal of a denied Medicaid application before an administrative law judge.

### The Importance of Timing

Another important Medicaid rule is that the individual must meet all of the Medicaid eligibility criteria on the first day of the month to receive any help that month. It is essential that the planner have complete and accurate information concerning the assets owned by the potential Medicaid applicant and his or her spouse. Spending down assets must be carefully timed to meet this first-of-the-month rule.

### Planning Ahead – The Key to Security

No two persons' circumstances are exactly alike, so the process of planning for incapacity is very individualized and personal. Careful and advance planning can help assure that both you and your loved ones' wishes are carried out and that you are protected and able to get life's business done - even when the unexpected happens.

**Severns and Bennett** are a team of experienced law professionals who are located in Indianapolis, IN. For more information, you may contact them at (317) 633-4090 or log on to their website at [www.severns.com](http://www.severns.com).



### A Decade of Research

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In addition, researchers were also able to consistently demonstrate that the Apolipoprotein E2 allele is a protective factor reducing the risk for AD. It is important to note that all these studies have consistently shown that while alleles or forms of the Apolipoprotein E gene can increase or decrease the risk for Alzheimer disease, they do not cause Alzheimer disease.

A number of Alzheimer disease researchers have also sought in recent years to identify additional genetic risk factors for late onset Alzheimer disease. In a number of studies, there has been consistent evidence of a gene contributing to the risk for Alzheimer disease on chromosomes 10 and 12. At

the recent 8th International Conference on Alzheimer's Disease and Related Disorders in Stockholm, Sweden, a number of research groups reported progress toward the identification of these genes.

Another area that Alzheimer disease researchers have focused their efforts on is a better understanding of the factors that contribute to the age at which an individual develops Alzheimer disease. It is thought that one set of genes may affect whether or not an individual develops Alzheimer disease and another set of genes may determine the age at which an individual begins to develop symptoms of disease. A number of researchers have begun to study this question which has made it even more important for

us at the National Cell Repository to obtain accurate information about an individual's age at onset of dementia.

As you can see, the families participating in the National Cell Repository have had a great impact on our understanding of the genetics of Alzheimer disease. We appreciate everyone's active participation in this important research project.

In a previous issue of the National Cell Repository newsletter, we published an article about the genetics of Alzheimer disease. If you would like to receive another copy of this article or a complete list of references, please contact the National Cell Repository staff at 800-526-2839.

# One Family's Experiences with

“**W**anted, families with two or more persons with Alzheimer’s Disease.” With my response to this advertisement, I became involved in a study at Indiana University. My mother and her sister had the disease and another sister had early, but unmistakable symptoms. During the past fifteen years, I have provided genealogical information and my blood, tried to coax a reluctant brother and father into providing blood samples, and have seen that an aunt’s autopsy was performed and brain tissue samples were provided to the study. Indiana University adds the blood samples, brain samples and genealogical information to the National Cell Repository. These DNA samples are sent to researchers worldwide, upon request. Although it is a periodic reminder of things I would prefer to forget, this small contribution to an Alzheimer’s research project seems the least I can do.

Our family’s introduction to Alzheimer’s disease began with my mother. Before 1960, Mother was a well beloved college English professor, approaching her fifties. She lived her life fully in the present, postponing nothing for the future. Gradually, late in this time period, people began to notice things that were out of character for her: wasting too much time in colleagues’ offices, or not considering it important to get to class on time. During the summer of 1960 she spent four weeks with us and made me uneasy when she announced she had given up reading for Lent. I remember going home over Thanksgiving of 1960 and realizing that she hadn’t graded any weekly freshman English papers yet that semester. Even more surprising, it did not bother her any more than going late to class did. The Dean was finally paying attention to the increasing complaints and asked her to resign.

In January 1961, at age 50, Mother was hospitalized and dye was inserted into her spine. Resulting tests of the brain indicated early-onset Alzheimer’s disease, a term not then generally used. (Initial identification isn’t nearly as invasive now. Today it consists of tests to gauge thinking and remembering abilities and

identification of other treatable problems with similar symptoms.) In 1961 this was a disease which none of the family or community had heard of, and which the specialist doctor diagnosed, but could not treat. The doctors didn’t tell the family what to expect, either physically or socially.

My parents had a party later in that month after mother’s diagnosis. On the day of the party, Mother threatened not to let anyone in who had voted for Senator Kerr. This outburst came from a woman not even interested in politics. This was their last party. Daddy felt uncomfortable taking her into social situations, even with long time friends. Eventually he also sorted out family who weren’t comfortable with a visit.

As Mother’s condition slowly progressed, my father returned purchases to door-to-door salesmen, put a fence around the back yard to prevent Mother from wandering away, and finally retired early to take care of her. She became more and more quiet. Finally she deteriorated to where she knew no one and didn’t get out of bed. Ultimately, she lived sixteen years after being diagnosed.

Amusing things remain among my memories. She visited us two years after her diagnosis. We went to dinner at a friends’ house, although Mother didn’t know them. She was silent all evening until the conversation turned to the discussion of “what was the name of that book?” At this point she uttered her only words of the evening. In a rather disgusted tone, resulting from the obvious general ignorance, she said “Ethan Fromm.” The correct comment, coming from her professional past, was greeted with shock and surprise at the sudden contribution, even though we all knew that she was ill.

My father’s best qualities were emphasized as he cared for her. He had always lived for future vacations. Now he combined his interest in travel with accommoda-

# Alzheimer's Disease

Anonymous

tions that enabled him to keep a close eye on her activities. He complained very little considering the circumstances. In fact, he enjoyed himself in spite of the frequent trying situations.

“Do you know where Mother is?”

“No. If she isn't upstairs, we need to look for her again.”

“She isn't there. You check the back alley and I'll check the neighbors.” That time she was found in our neighbor's house up the hill three or four doors. She sat at the kitchen table of a perfect stranger while he had his beer and she had her coffee. The wife of the house kept an eye out for me, or whoever turned up looking for this unexpected visitor. This panic-laden event repeated itself in spite of all vigilance. At times Mother slipped off from my parents' camper, perhaps in her slip. We soon learned she was likely to go downhill, that the closest coffee shop or bar was a preferred destination and that the police were helpful.

As my brothers and I reached fifty, we each privately wondered if this might happen to us, too. One day, when we were together, this concern came up in conversation and each of us admitted to the anxiety.

The next member of the family to show Alzheimer's symptoms proved to be mother's older sister. I lived near my aunt and watched the disease progress, still without treatment, but with more outside custodial care available. She didn't begin to have symptoms until her mid-seventies, when she was twenty years older than mother had been at onset, and many years after her retirement as a college teacher. Because she had watched her sister go through Alzheimer's, my aunt was fearful of the obvious future. She never stated her fear, even upon diagnosis, but the haunted look in her eyes each week when we left her house communicated her fear well.

By this time I began participation in the Indiana University study. My aunt helped with the extensive genealogical details requested.

Later, when she was in a nursing home, she supplied a blood sample for the study, although she didn't know why the nursing home's technician was taking blood. When she died, an autopsy was done to confirm diagnosis (still the only way to know for sure if one has Alzheimer's) and to supply brain tissue samples to Indiana University's database. Nursing homes are very paranoid about autopsy, I discovered. They feel the desire for an autopsy means you think they did something wrong in treatment and care.

My mother's youngest sister is now showing symptoms of Alzheimer's. She takes new medications in an effort to retard progress of this disease. She, too, was in her mid-seventies when she began to show strong symptoms of the disease and hasn't actually verbalized her all too apparent and justified fears.

At one point in his early thirties, our son expressed concern about having children. From his perspective, he might just be passing on this disease. We now share the most recent glimmer of understanding from the news or current research. We hope there will be a breakthrough before either of us needs it. I took out long-term care insurance as soon as it became dependably available. I also work as a volunteer for the Alzheimer's Association.

Indiana University sends out a family update annually. It requests updates on family deaths, together with the cause of death, and any information on onset of Alzheimer's in additional family members. And, I wonder, who will be next and when.

# Research's Corner

By Amanda Myers

**A**lzheimer's disease (AD) is a genetically complex disorder. Following years of study, researchers have made important progress understanding the genes that affect the risk for familial AD. Initial studies focused on families with what has been called early onset AD. In these families, members develop the symptoms of dementia and AD before the age of 65. Intensive study of these families identified three genes whose DNA sequence is altered (or mutated). In these families, members with early onset AD have inherited a change in one of these three genes. These genes are called amyloid precursor protein (APP), presenilin-1 (PS-1), and presenilin-2 (PS-2). Families have also been studied in which members develop AD after the age of 65. The AD in these families is often called late onset AD. An important gene, apolipoprotein E (APOE), is a major risk factor leading to both early onset and late onset AD.

With the identification of these four genes, scientists have carefully studied why changes in these genes can increase the risk for AD. Study of the brains of individuals with AD has identified very characteristic changes. These include both plaques and tangles. The plaques are made up of many different substances, including beta-amyloid. All four of the genes identified thus far as important in AD act by influencing beta-amyloid.

Our lab has been interested in identifying more novel genetic AD risk factors. We have focused primarily on late onset familial AD. Our studies have examined the DNA from siblings, both of who have been found to have AD. The National Cell Repository identified some of the siblings we are currently using in our research studies. As you know, we do not know the names or any other identifying information about the samples we are using. In this way, we do not know whose DNA we are using in our study of AD. However, we have found it most useful in our experiments to use DNA from siblings who have been carefully examined by a neurologist or other AD specialist and determined to have probable AD. We also prefer to study families in which at least one member has had an autopsy confirming the diagnosis of AD. We believe that this ensures our studies have the greatest power to identify genes for AD.



## Members of the research lab team

**From left to right - Back row:** Bill Wu, Scott Smemo, Paul Pastor, Shantia Shears, Joanne Norton, Heather Stock  
**Middle row:** Emily Walker, Anne Brunkan, Petra Nowotny, Silva Hecimovic, Jun Wang, Denise Levitch  
**Front row:** Jan Konrad, Maribel Martinez, Alison Goate, Jen Wang, Sumi Chakraverty

So far, we have found evidence that there may be a gene for AD on chromosome 10. While we have not yet isolated the gene responsible for the effect on chromosome 10, we at least now have a clue as to where to look. When this risk factor gene is found, it might potentially elucidate new genes and/or pathways involved in the development of AD, thereby providing an alternate route for the treatment of AD.

**Amanda J. Myers**, graduate student, Division of Neuroscience, Washington University

**Alison M. Goate**, D. Phil, Departments of Psychiatry and Genetics, Washington University

## We Have Changed Our Name, But Not Our Mission!

Until recently, the National Cell Repository was part of the Indiana Alzheimer Disease Center (IADC). In July 2002, the Repository was renamed the **National Cell Repository for Alzheimer's Disease** and it is no longer part of the IADC. This was an administration change. There has been no change in procedures, where samples are stored, or our telephone number and staff. Our goal remains to assist researchers in understanding why people develop Alzheimer disease so that more effective treatments can be developed to stop this devastating disease.

# Research Opportunities

## Study of Aripiprazole in the Treatment of Patients with Psychosis Associated with Dementia of the Alzheimer's Type

- Purpose: To learn if aripiprazole is safe and effective in the treatment of psychosis associated with dementia of the Alzheimer's type.
- Eligibility: 55-95 years old, both genders, institutionalized with AD
- Locations: CA, FL, TN, VT, WI
- Contact Information: Bristol Myers Squibb (203) 677-6000

## Healthy Aging and Memory Study

- Purpose: This project will focus on the development and testing of efficient, cost effective measures that are specifically designed for use in AD primary prevention trials. The new or improved measures that have been developed will then be evaluated in 650 nondemented subjects enrolled in a simulated Alzheimer's disease prevention trial. Once enrolled, subjects will be followed for four years with annual clinical evaluations and interim six-month phone calls.
- Eligibility: 75+, both genders
- Locations: AL, AZ, CA, CT, DC, FL, GA, IL, IN, KY, MD, MA, MI, MN, MO, NV, NY, OR, OH, PA, RI, SC, TX
- Contact Information: Call Jami Stuck at 800-526-2839 for specific contact information

## Treatment of Agitation/Psychosis in Dementia/Parkinsonism (TAP/DAP)

- Purpose: To determine the efficacy (as well as safety, tolerability, and influence on parkinsonism) of quetiapine and donepezil, used alone or in combination, for the treatment of psychosis and/or agitation in patients with primary dementia complicated by coexistent parkinsonism.
- Eligibility: 50+, both genders, diagnosis of AD, symptoms of psychosis, agitation, parkinsonism
- Locations: AL, AZ, CA, GA, IL, MD, MA, MI, NV, NY, PA, TX, VT, WA
- Contact Information: Kimberly Schafer, M.S. PH: (858) 622-5863 E-mail: kschafer@ucsd.edu

## CATIE-Alzheimer's Disease Trial

- Purpose: To determine whether three antipsychotic medications (olanzapine, quetiapine, and risperidone) help prevent behavioral and psychiatric concerns in patients with Alzheimer disease.
- Eligibility: Diagnosis of Alzheimer disease, presence of psychiatric disturbances (i.e. hallucinations, delusions, agitation)
- Locations: AL, CA, CT, FL, GA, HI, IL, IA, LA, MD, NY, NC, OH, PA, SC, TX
- Contact Information: Karen Dagerman, PH: (323) 442-3715

## Estrogen Effects on Memory Functioning in Post-Menopausal Women and Patients With Alzheimer's Disease

- Purpose: To examine whether three months of estrogen administered to 1) post-menopausal women and 2) women with mild-moderate Alzheimer's disease who are concurrently treated with standard therapy, will enhance the system in the brain involved in memory and learning.
- Eligibility: Healthy post-menopausal women ages 50-60 and 70+ AND post-menopausal women with mild-moderate AD ages 45+
- Location: Participants must be within reasonable driving distance to Burlington, VT.
- Contact: Sally Ross Nolan, M.S. PH: (802) 847-9488 E-mail: Sally.Nolan@vtmednet.org

## African-American Dementia and Aging Project (AADAPt)

- Purpose: To determine the incidence and specific risk factors for age-related problems, such as memory loss, among African Americans.
- Eligibility: ages 65+, normal or mild cognitive decline
- Location: Portland, OR
- Contact Information: Pamela McNeal, PH: (503) 494-2367, E-mail: mcnealp@ohsu.edu

## Efficacy And Safety Of CX516 In Elderly Participants With Mild Cognitive Impairment

- Purpose: There is evidence CX516 enhances brain activity by specifically targeting remaining glutamate receptors in the affected portions of the brain. This study will test the safety and efficacy of CX516 in the symptomatic treatment of participants with mild cognitive impairment.
- Eligibility: 55-85 years old, mild cognitive impairment
- Locations: AZ, CA, CT, FL, IA, PA
- Contact Information: Lien Beamon, PH: 919-544-3170 x 5118 E-mail: Lien.Beamon@parexel.com

## Alzheimer's Disease Anti-Inflammatory Prevention Trial (ADAPT)

- Purpose: To study the ability of naproxen and celecoxib (non-steroidal anti-inflammatory medications) to delay or prevent the onset of AD and age-related cognitive decline.
- Eligibility: Healthy, ages 70+, family history of dementia (i.e. AD)
- Locations: AZ, MD, MA, NY
- Contact Information: Chris Szekely, PH: 866-2STOP-AD (toll free)

## Alzheimer's Disease Prevention Trial

- Purpose: To determine whether estrogen and progesterone can delay the onset of memory loss or AD in elderly women with a family history of the disease.
- Eligibility: Healthy, ages 65+, family history of dementia
- Locations: AL, CA, CT, DC, FL, MD, NY, MD, NJ, NY, NC, OK, RI, SC,
- Contact Information: Evelyn Dominguez-Rivera, PH: (212)305-5805

## Sources for Information and Support

### Alzheimer's Association

<http://www.alz.org>  
Tel: 312-335-8700 or 800-272-3900

### Alzheimer's Disease Education and Referral Center (ADEAR)

<http://www.alzheimers.org>  
Tel: 301-495-3311 or 800-438-4380  
‡ ADEAR lists all 29 Alzheimer  
Disease Centers (ADCs) and their  
contact information.

### Depression and Related Affective Disorders Association

<http://www.med.jhu.edu/drada>  
Tel: 410-955-4647

### Family Caregiver Alliance

<http://www.caregiver.org>  
Tel: 415-434-3388 or 800-445-8106

### National Parkinson Foundation

<http://www.parkinson.org/>  
Tel: 305-547-6666 or 800-327-4545

### Parkinson's Disease Foundation (PDF)

<http://www.parkinsonsfoundation.org>  
Tel: 212-923-4700 or 800-457-6676

### Society for Progressive Supranuclear Palsy

<http://www.psp.org>  
Tel: 410-486-3330 or 800-457-4777

### National Organization for Rare Disorders (NORD)

<http://www.rarediseases.org>  
Tel: 203-746-6518 or 800-999-NORD  
(6673)

### Creutzfeldt-Jakob (CJD) Foundation Inc.

<http://cjdffoundation.org>  
Tel: 954-704-0519 or 305-891-7579

## 10 Signs of AD

1. Memory loss.
2. Difficulty performing familiar tasks.
3. Problems with language.
4. Disorientation to time and place.
5. Poor or decreased judgment.
6. Problems with abstract thinking.
7. Misplacing things.
8. Changes in mood or behavior.
9. Changes in personality.
10. Loss of initiative.

If you recognize several of these warning signs in yourself or a loved one, the Alzheimer's Association recommends consulting a physician. Early diagnosis of Alzheimer's disease or other disorders causing dementia is an important step in getting appropriate treatment, care, and support services. **For more information, call the Alzheimer's Association at (800) 272-3900.**



INDIANA UNIVERSITY  
SCHOOL OF MEDICINE

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