Ron strongly believed in our mission to understand alcoholic pathology and develop ways to treat it. Our greatest tribute to Ron will be to make this happen.

—Fulton Crews, Director, Bowles Center for Alcohol Studies

Yes, I would like to honor Ron's memory with a donation.

❑ $100 ❑ $250 ❑ $500 ❑ other _____

❑ $1000 *Bowles Club* ❑ $2000 *Chancellor's Club*

❑ Check enclosed, payable to the Bowles Center for Alcohol Studies

❑ I would like to transfer stock, please send information

❑ My company matches gifts. The form is attached.

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The Ronald G. Thurman Lectureship Award

For more information please contact Elizabeth M. Amend

1-919-843-6304

amend@unc.edu

Ron Thurman, doktorvater

—a eulogy by Gavin Arteel

"Ron emphasized that the work we do does not exist independently from society as a whole."

Some words in German are more expressive than their counterparts in English. For example, the word for 'dissertation advisor' in German is 'doktorvater,' which translates literally to 'doctor-father.' This word clearly implies an almost parental aspect in the relationship between mentor and student. I met Ron Thurman in 1993 when he served as my dissertation advisor, or more accurately, as my doctor-father. Ron took it as a personal challenge and responsibility to train and guide young colleagues to become better scientists. As doctor-father, Ron practiced tough love. Never a subtle man, he was perfectly willing to give the verbal kick in the nether regions when he thought we needed it. At the same time, he was highly enthusiastic and supportive of our work.

Ron valued communication in the highest and always kept himself informed of our progress by weekly, daily—sometimes hourly—one-on-one meetings. However, he was never heavy-handed in controlling the projects. He was always approachable and willing to entertain new ideas and give us the means and resources to chase them down. He made it very clear that the projects were ours to do and ours to develop, and he gave us the freedom to take initiatives.

Ron always referred to the Thurman lab as 'the team' and we did indeed feel like a team. His enthusiasm for science was infectious. Often he would return from conferences and meetings with a notebook full of ideas, eager to discuss possible new avenues of research for the team.

Ron was famous for one-line comments to his students and colleagues designed to cut to the quick. We often heard "where's the data?" and "what's the hypothesis?" Sometimes he interrupted long-winded explanations with "put the scheme on the board." But my personal favorite was, "so what?" "So what" implied a host of questions, including "what do these data mean?, what's the next experiment?, what's the significance of this work?" and "how do these data fit into our current working hypothesis?" Asking "so what" forced you to think more clearly, to relate your work to the big picture, and helped you to organize any project at its inception. Ron emphasized that the work we do does not exist independently from society as a whole.

With his untimely departure, Ron leaves a vacuum in the lives of many. I will always value and be affected by his mentoring. It was a privilege to know him and learn from him. I take it as a personal challenge to live up to his example. He will be missed.—Gavin Arteel

Where's the data? What's the hypothesis? So what?

A Brilliant Scientist, A Great Friend

Fulton T. Crews, Director, Bowles Center for Alcohol Studies

Ron Thurman had smiling eyes, a brilliant mind and a delightful sense of humor. Ron and I had become very close over the last several years through collaborations, student co-mentoring, and sharing our discoveries about alcoholism, gene delivery, and molecular mechanisms of cell activation and death. The study of alcoholic pathology is challenging and fascinating. Ron and I loved to educate each other about alcohol's effects on different tissues, shared mechanisms and common cell signaling. Ron was an original thinker. To this day, I remain awed by his discovery of glycine channels in the liver—and that dietary glycine reduces alcoholic liver damage. This is fun science, and making science fun was one of Ron's greatest gifts.

He was also gifted in his charm, humor, and love and knowledge of fine food and wine. He always had a joke for his friends. All who knew him—we in the Center, the many departments and curricula in UNC that depended on his teaching abilities, and liver researchers around the world—will always remember Ron with fondness and respect.

His two senior proteges carry on his work at UNC, continuing to make discoveries that are likely to lead to new and improved treatments for liver disease. From Ron they acquired not only scientific knowledge, but a love for science and his brilliant way of asking the important questions. Gavin Arteel has developed a model of alcoholic pancreatitis, used knockouts to dissect key genes in alcoholic liver disease and used green tea (a source of anti-oxidants) to block liver pathology. Mike Wheeler has used a variety of genes to block liver pathology. His use of gene delivery technology has incredible future potential, and Mike is on the cutting edge. Ron's colleagues in the Center's liver pathology group—John Lemasters, David Brenner, Richard Rippe and Michael Fried—continue exploring hepatic gene regulation, cell death and human liver disease progression.

Over a year ago I wrote a column in this newsletter focused on Ron's work and noted that every basic scientist's dream is to make great leaps in treating human disease. Ron strongly believed in the Center's mission to understand alcoholic pathology and develop ways to treat it. Our greatest tribute to Ron will be to make this happen.

The Ronald G. Thurman Lectureship Award
Bowles Center for Alcohol Studies, School of Medicine, University of North Carolina at Chapel Hill
CB 7178, Chapel Hill, NC 27599-7178. Contact Elizabeth Amend, amend@unc.edu

Ron Thurman, Ph.D.

A Scientist's Scientist ▪ Mentor ▪ Colleague ▪ Friend

1941 - 2001

On July 14, 2001, the alcohol research community lost a leader with the death of Ronald G. Thurman, Professor of Pharmacology and Director of the Laboratory of Hepatobiology and Toxicology.

Thurman came to the University of North Carolina at Chapel Hill in 1977 after completing his education. He completed his Ph.D. in Pharmacology at the University of Illinois Medical College and postdoctoral training with Britton Chance at the University of Pennsylvania and Roland Scholz at the University of Munich.

From the beginning of his research career, Ron Thurman focused his attention on liver disease, a frequent consequence of alcoholism and the cause of more than 26,000 deaths annually in the United States. Thurman was known for his brilliant, practical, and thorough approach to scientific problems. He was respected not only among US researchers, but also among the global research community. He maintained active collaborations with laboratories in Germany and Japan; several colleagues traveled from Japan to attend Thurman's memorial service at the University of North Carolina.

"I see little difference between my research goals and my role as an educator. It is my aim to encourage graduate students to gather data sufficient for them to appreciate how exciting biomedical research can be."
—Ron Thurman

At the UNC memorial service, Ron Thurman was described by Professor Rudy Juliano, Chair of Pharmacology, as a scientist's scientist. This description embodied his devotion to science, his creativity and talent to make new discoveries, to uncover mechanisms and to identify the critical missing factor in a scientific problem. His colleagues also spoke of his tremendous integrity and his many contributions to our School of Medicine as professor, mentor, teacher, and colleague as well as one of our best scientists. Faye Calhoun of the National Institute of Alcohol Abuse and Alcoholism (NIAAA) spoke of Thurman's many contributions to the work of the NIAAA. She described his remarkable abilities to critique, to discover, to lead and to support as blessings to all of the staff of NIAAA. Many of Thurman's students and collaborators spoke profoundly about his care for their scientific development. One student wrote a poem about Ron's impact on the lives of those in his laboratory. Thurman's colleagues were truly his scientific family. Many colleagues dearly miss him.

If Ron Thurman had one talent more recognized than others, it was his ability to mentor others well. Ron mentored many other faculty, postdoctoral fellows, as well as students. Over the course of 30 years at UNC, Ron hosted and trained hundreds of scientists. Ron's style of mentoring combined his enthusiasm, vast knowledge and integrity with high expectations and an insistence on scientific rigor. His leadership and example made working in the Thurman lab a sure path to successful independent research. As he once stated, "I see little difference between my research goals and my role as an educator. It is my aim to encourage graduate students to gather data sufficient for them to appreciate how exciting biomedical research can be."

The Ronald G. Thurman Lectureship Award

The Ronald G. Thurman Lectureship Award has been established by the Bowles Center for Alcohol Studies, School of Medicine, University of North Carolina to honor the scientific excellence of Dr. Thurman's research and teaching. This Award will commemorate Ron's life—not only for those of us who benefited in so many ways from knowing him—but also for the students and scientists that will follow in his path.

A distinguished researcher contributing to our knowledge of alcohol and liver function will receive the Award. The awardees will be invited to visit the Center, present a lecture and meet with our investigators to share knowledge and new ideas. A plaque recognizing Ron and listing the names of all awardees and donors will hang in the Center's lobby.

With your support this endowed award will become a reality in 2002. Our goal is a minimum of $100,000. Each awardee will receive up to $5,000 to support travel expenses and an honorarium. The Ronald G. Thurman Lectureship Award will serve to generate excitement and focus greater attention on the vitally important research that was Ron's passion.

Attached is your gift card. If you would like more information, please contact Elizabeth Amend at 919-843-6304 or amend@unc.edu. You can also visit our website, www.med.unc.edu/alcohol.

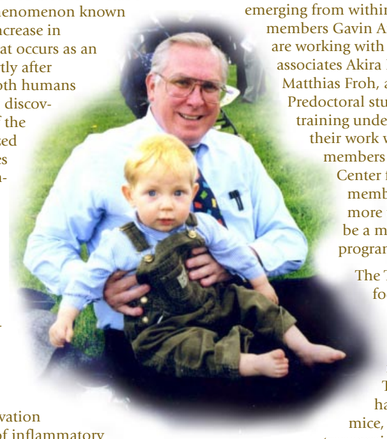
Each of you honoring Dr. Thurman will be recognized in a special section of our newsletter, *Center Line* and on the plaque.

Emphasis on international cooperation and collaboration

Ron Thurman's expertise spanned the fields of gastroenterology, toxicology, and pharmacology. He was active in numerous scientific organizations including the American Gastroenterological Association, the American Association for the Study of Liver Diseases, the Society of Toxicology, and the Research Society on Alcoholism. Thurman was also instrumental in founding the International Society for Biomedical Research on Alcoholism—another example of his emphasis on world-wide cooperation and collaboration. Shortly before his death, he had assumed the role of associate editor of the international journal *Gastroenterology*.

Advancing the understanding of the pathophysiology of alcoholic liver disease

Over the years, Ron Thurman and his laboratory made several ground-breaking contributions to the understanding of alcoholic liver disease. For example, they characterized alcohol metabolism—particularly a phenomenon known as SIAM, or the swift increase in alcohol metabolism that occurs as an adaptive response shortly after alcohol ingestion in both humans and animals. They also discovered the importance of the Kupffer cell, a specialized liver cell that eliminates toxins, in the pathogenesis of alcoholic liver disease. They found that, while under normal conditions the Kupffer cell protects the liver through its toxin-eliminating activity, it may contribute to liver pathology under conditions of chronic alcohol use. Chronic alcohol use causes Kupffer cell activation with resultant release of inflammatory mediators such as tumor necrosis factor alpha. When activated by chronic alcohol, Kupffer cells stimulate metabolic overdrive, eventually causing lack of oxygen in the liver. The oxygen deficit is believed to be one factor involved in the death of liver cells that occurs in liver disease. Work reported by the Thurman laboratory in the mid-1990s supported this hypothesis by showing that destroying Kupffer cells can prevent alcohol-induced liver injury.



Thurman and his laboratory also found that chronic alcohol drinking causes endotoxin, a toxic substance released by human intestinal bacteria, to penetrate the intestinal walls more easily than under normal conditions. Chronic exposure of Kupffer cells to the "liberated" endotoxin causes Kupffer cell activation and the release of inflammatory substances that injure the liver. In more recent efforts, Thurman and his laboratory used gene delivery and knock-out mice to elucidate the roles of particular inflammatory substances in promoting liver injury during chronic alcohol exposure.

Research being carried forward by colleagues and emerging leaders from the team

Ron Thurman's discoveries and innovations are described in more than 400 scientific publications appearing over a 30-year period. Last year, Thurman received a NIAAA Merit Award for his role in elucidating the mechanisms of injury in alcoholism. His research has changed the way scientists conceptualize and study liver disease, and is helping to point the way to means of mitigating or preventing liver disease in alcoholism. Thurman's laboratory continues this work today.

The research program that Thurman established is being continued by his team. Regular lab meetings have been re-established and new leadership is emerging from within the group. Junior faculty members Gavin Arteel and Michael Wheeler are working with senior postdoctoral associates Akira Konno, Fuyumi Isayama, Matthias Froh, and Erwin Gaebele. Predoctoral students who had been training under Thurman are continuing their work with the help of senior members of the lab and other Bowles Center faculty. Blair Bradford, a member of the Thurman team for more than 20 years, continues to be a mainstay of the research program.

The Thurman team continues to focus on the role of oxidants in early alcohol-induced liver injury. In addition to studying rats in the enteral model developed by Tsukamoto and French, they have modified the model for mice, so that knockout and transgenic mice can be employed. Using this model they have developed a working hypothesis of the precise mechanism that leads to liver damage. As mechanisms are identified, the team applies the knowledge to test targeted strategies against alcohol-induced liver injury. These strategies include antioxidant and gene delivery approaches that have both heuristic and therapeutic potential.

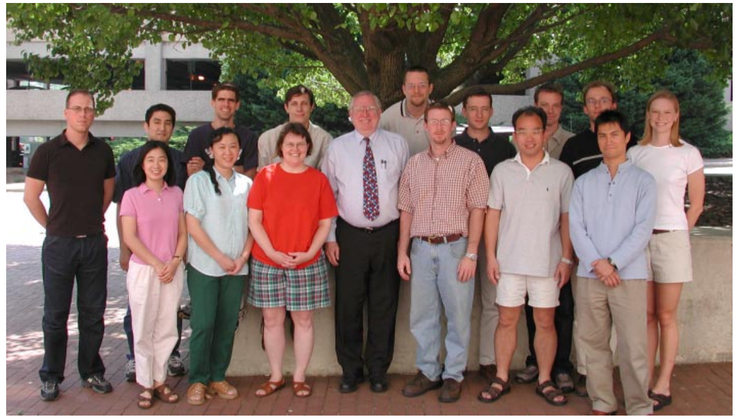
Other projects are investigating the mechanisms by which alcohol consumption causes fibrosis in liver using long-term ethanol administration (up to 4 months). Associate professor Zhi Zhong and post-doctoral fellows Lars Conzelmann and Mark Lehnert are interested in the mechanisms of alcohol-induced fatty liver graft failure following liver transplantation. Other projects seek to understand the mechanisms of hepatic carcinogenesis due to nongenotoxins in mice.

From left to right, Drs. Kenichi Ikejima, University of North Carolina at Chapel Hill; Hide Tsukamoto, University of Southern California; Ron Thurman; and Anna Mae Diehl, Johns Hopkins School of Medicine.

(Below) Standing next to Ron is Dr. Nobuhiro Sato, Juntendo University School of Medicine; seated are Drs. Michael Arthur , University of Southampton School of Medicine (left) and David A. Brenner, UNC-CH (right).

Arteel and Wheeler are also developing new research programs with the assistance of other UNC faculty, notably David Brenner and Jude Samulski. Arteel has recently received funding from NIAAA to investigate mechanisms of chronic pancreatitis due to alcohol abuse. Wheeler has been developing recombinant adeno-associated viral serotypes to develop better gene delivery for alcoholic liver disease. These young investigators mirror Ron's enthusiasm for science.

Thurman's legacy lives on in the lives and work of the hundreds of postdoctoral fellows, graduate students, laboratory technicians, and collaborators who carry on his tradition of excellence and innovation in research.



Ron Thurman's laboratory, Spring of 2001. Front row from left to right: Xiangli Li, Zhi Zhong, Blair Bradford, Ron Thurman, Mike Wheeler, Takehiko Uesugi, Fuyumi Isayama. Back row: Lars Conzelmann, Akira Konno, Brian Dewar, Ivan Rusyn, Gavin Arteel, Erwin Gaebele, Matthias Froh, Mark Lehnert, Olivia Smutney.

The Ronald G. Thurman Lectureship Award
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