

10-27-1995

## NEWS AND NOTES 1995, VOL.6, NO.7

The Rockefeller University

Follow this and additional works at: [http://digitalcommons.rockefeller.edu/news\\_and\\_notes\\_1995](http://digitalcommons.rockefeller.edu/news_and_notes_1995)

---

### Recommended Citation

The Rockefeller University, "NEWS AND NOTES 1995, VOL.6, NO.7" (1995). *News And Notes 1995*. Book 19.  
[http://digitalcommons.rockefeller.edu/news\\_and\\_notes\\_1995/19](http://digitalcommons.rockefeller.edu/news_and_notes_1995/19)

This Book is brought to you for free and open access by the The Rockefeller University News and Notes at Digital Commons @ RU. It has been accepted for inclusion in News And Notes 1995 by an authorized administrator of Digital Commons @ RU. For more information, please contact [mcsweej@mail.rockefeller.edu](mailto:mcsweej@mail.rockefeller.edu).

## Japan awards cultural honor to Hanafusa

The Japanese government will present Japan's Order of Culture to cancer researcher Hidesaburo Hanafusa, Leon Hess Professor at Rockefeller, in a ceremony at the Imperial Palace in Tokyo Fri., Nov. 3.

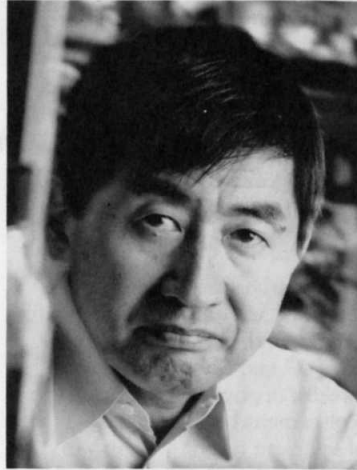
Hanafusa is the only scientist of the five native Japanese receiving the annual international prize known as the Bunka Kunsho, which honors individuals for their artistic or scientific contributions to world culture. The award is a medal embossed with a chrysanthemum, symbol of the Japanese royal family.

"We congratulate Dr. Hanafusa on receiving this wonderful recognition, the Japanese Order of Culture, for his contributions to identifying oncogenes as well as determining their structure and function," said Torsten N. Wiesel, president of Rockefeller. "We are all proud and pleased to have Dr. Hanafusa as a member of our faculty."

Hanafusa's investigations focus on oncogenes, which can transform normal cells to cancerous ones. For his scientific achievements, Hanafusa previously received a Sloan Prize, a Lasker Award, and the Japan Culture Merit Award.

Hanafusa joined RU in 1973 and his early studies confirmed that oncogenes exist in all normal animal cells. Since then, investigators in many groups including Hanafusa's have identified more than 40 oncogenes.

In his work, Hanafusa noted that tumor-causing viruses stripped of all the genetic material needed to form tumors still induced cancer in animal cells. Hanafusa found the viruses reacquired the missing oncogene from the cells' normal genetic mate-



**Professor Hidesaburo Hanafusa** previously received a Sloan Prize, a Lasker Award, and the Japan Culture Merit Award.

rial. The experiments also demonstrated that the viruses used the oncogene to produce tumors by inappropriately stimulating normal cell genes to overproduce their protein products. In these experiments, Hanafusa used the Rous sarcoma virus, named for its discoverer Peyton Rous, a Rockefeller scientist

and Nobel laureate.

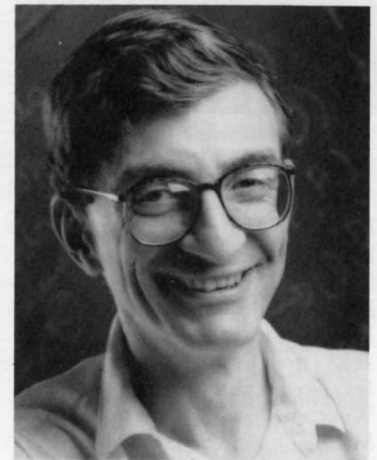
Hanafusa's current research focuses on the structure and function of oncogenes, the proteins they make, and how these genes regulate other genes in a cell. Some oncogene proteins are enzymes that regulate basic cell functions. His group analyzes the biochemical properties of such enzymes and how they influence cell growth and metabolism.

Recently, one of these studies led to the discovery of particular protein domains, named SH2 and SH3, which play pivotal roles in protein interactions related to cell growth. Understanding the cell functions of oncogenes is key to elucidating the processes involved in cancer.

A native of Nishinomiya, Japan, Hanafusa received his B.S. in 1953 and a Ph.D. in biochemistry in 1960, both from Osaka University. He is a foreign associate in the U.S. National Academy of Sciences and an honorary member of the Japanese Cancer Association. He also is a member of numerous scientific societies, including the American Society of Microbiology,

See *Hanafusa*, page 4

## RU professor evaluates Earth's population limits



**Professor Joel E. Cohen's** new book on Earth's carrying capacity was excerpted in the November/December issue of *The Sciences*.

Rockefeller Professor Joel E. Cohen, head of the Laboratory of Populations, raises the question "How Many People Can the Earth Support?" in the Friday lecture today (Oct. 27).

Cohen, a population biologist and applied mathematician, studies the ecology, epidemiology, demography, and social organization of populations—from cellular to human—using mathematical models and quantitative data. Currently, his research focuses on the complexities of global population growth, infectious disease in Latin America, and the ecology of food webs. In combination with mathematical models that project human population growth rates, he explores how cultural, economic, and environmental variables affect future population size.

According to Cohen's soon-to-be-published book, *How Many People Can the Earth Support?*, the world's population has increased a thousandfold in the last 10,000 to 12,000 years. If fertility rates remain at the 1990 level, the global population will exceed 694 billion by the year 2150, more than 12,000 humans for every square mile of dry land. Cohen believes that the number of people the earth can support depends on the interaction of nat-

See *Cohen*, page 4

### At the fall meeting

#### RU Council receives dispatch from war on bacteria



Professor Alexander Tomasz (right) and Barry Kreiswirth, director of the Public Health Research Institute's (PHRI) Tuberculosis Center, spoke together at the fall meeting of the RU Council Thurs., Oct. 19. Nearly 200 friends of the university attended the program, entitled "Reinventing Antibiotics: Developing New Medical Strategies in an Age of Bacterial Resistance." To combat the spread of antibiotic resistance, Kreiswirth, Tomasz, and Richard B. Roberts, vice chairman of the Department of Medicine at New York Hospital-Cornell Medical Center, have formed an initiative called Bacterial Antibiotic Resistance Group-Infectious Diseases Center. Roberts spoke at the meeting, as did Lewis M. Weinstein, PHRI president, and Professor Vincent Fischetti. David Rockefeller, council chair, welcomed the guests, and Richard M. Furlaud, chair of the Board of Trustees, Betsy McCaughey, Lieutenant Governor of New York, and President Torsten Wiesel also addressed the gathering.

2 Peaks and trees

3 A second chance

4 Flu shots for all

# RU lab hosts French microbiologist in visit to area scientists

Courtesy Philippe Sansonetti



**Philippe Sansonetti, professor at the Institut Pasteur, will give a lecture Tues., Oct. 31.**

Hosted by Assistant Professor Robert Masure, Philippe J. Sansonetti, head of the Unite de Pathogenie Microbienne Moleculaire at the Institut Pasteur, will stay at RU from Mon., Oct. 31 through Fri., Nov. 3. through the Burroughs Wellcome Visiting Professorship in Microbiological Sciences. At the Wellcome Lecture Tues., Oct. 31, Sansonetti will discuss "Molecular and Cellular Mechanisms of Invasion of the Intestinal Epithelial Barrier by Enteric Pathogens: *Shigella flexneri* and Others."

"Dr. Sansonetti, an outstanding

scientist and an inspiring teacher, is one of the bright stars in the field of microbial pathogenesis and infectious diseases. He is a true physician-scientist, who begins his day with clinical work, then proceeds to his lab, where he directs some two dozen graduate students and postdoctoral fellows," said Masure. "We are delighted to have this opportunity to have him present lectures at four major institutions in New York."

During the week, Sansonetti will meet RU scientists and will give seminars at Albert Einstein College of Medicine, New York University (NYU), and the New York Public Health Research Institute. His host at NYU will be Arturo Zychlinsky, a recent Rockefeller graduate.

Sansonetti earned a M.D. in 1979 from the University of Paris. After completing a postdoctoral fellowship in enteric disease at the Walter Reed Army Institute of Research in Washington, DC., he joined the Institut Pasteur in 1981 as a research assistant. He became professor in 1994.

Among his awards are the Prix AGIR, awarded by the Pasteur-Weizmann Council, and the Grand Prix of the French Academy of Medicine.

The American Society for Microbiology (ASM) selected the

Laboratory of Molecular Infectious Diseases's proposal to the Burroughs Wellcome Fund to host Sansonetti in New York. The fund encourages applications from "institutions, including those with predominantly minority enrollments, newer campuses, and those located in less urban areas." The lab proposed sharing Sansonetti with other local institutions, thus reaching many minorities and individuals

who will be employed in coming years at newer and less urban campuses.

Begun in 1983, and administered by the ASM, the annual visiting professorship was established by Burroughs Wellcome to stimulate interest and encourage careers in the microbiological sciences.

Sansonetti's lecture will take place Tues., Oct. 31 at 3:45 P.M. in Caspary, with tea at 3:15 P.M.

## Plant Operations to replace ailing tree

Plant Operations will remove and replace a decayed London Plane tree adjacent to the 64th St. guard booth.

"Our arborist believes the tree was damaged years ago. Roughly 65 percent of the lower trunk is now hollow," said Robert A. Francis, director of physical facilities. "The replacement London Plane will be of sufficient height and girth to maintain the splendid appearance of the tree line in front of LARC."

Although the tree could possibly survive for another decade, "it would be a hazard," said Lulu Leibel, landscape coordinator. Wiring the tree for support is not an option because no anchor point is available on York Avenue nor on LARC. And, if the weakened tree, or its wiring, were to snap, pedestrians and guards would be at risk.

Removal is scheduled for later in

the season, and Leibel is searching for a replacement tree.

Anyone having questions or wishing to inspect the tree may call Francis, x8001.



**Decay has eroded the base of the tree.**

## Profile

### David J.E. Callaway

**Position:** Associate professor.

**Identity:** Theoretical physicist. Mountaineer. Athletic adventurer.

**On his postdoc at CERN:** "Sure, I took it for the prestige, great colleagues, all that. But being in the Alps didn't hurt."

**Accomplishments:** Scaling Mt. Everest. Competing in the Eco-Challenge in Utah last April, a 300-mile race that demanded mountain climbing, whitewater rafting, horseback riding, canoeing, and biking. "It was a chance to spend some time outdoors. It was also fun being on MTV and Dateline NBC."

**Eco-Challenge performance:** "Let's just say I didn't finish first, and second best is a loser."

**On climbing:** "Breathing is the hardest part. At 26,000 feet, you take four breaths between steps. With a headache from thin oxygen. And a misstep can mean death."

**On Mt. Everest:** "The trickiest thing about an Everest expedition is getting a permit from the

Nepalese government. And, of course, getting sponsorship. I'm organizing an expedition now. It's easy to get people to go to Everest. You call, and they say, 'when?'"

**Who says when:** "Old friends from the Central Intelligence Agency, Federal Bureau of Investigation, and Drug Enforcement Administration. A lot of physicists are good mountaineers, too."

Courtesy of David Callaway



**Associate Professor David Callaway pauses while ascending the Alps (left). Right: He horses around during the Eco-Challenge.**

**On similarities between physics and climbing:** "Both require effort, and the rewards are not pecuniary. You do both for the aesthetics. The point is, once you set a goal, you never give up. No matter what."

**Local pursuit:** Forming a Rockefeller group to climb up and ski down nearby peaks. "Science is nice but doesn't use everything you



can do. It's like keeping a Ferrari in a garage. You have to get out there."

Callaway may be reached at x8842 or email [callaway@summit.rockefeller.edu](mailto:callaway@summit.rockefeller.edu).

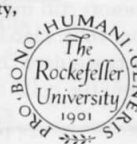
News&Notes is published each Friday throughout the academic year by The Rockefeller University, 1230 York Avenue, New York, NY 10021. Phone: 212-327-8967.

Torsten Wiesel, President  
Ingrid Reed,  
Vice President for Public Affairs and Corporate Secretary  
Marion E. Glick, Director of Communications

Kay Locitzer, Editor  
Joseph Bonner, Associate Editor  
Robert Reichert, Photography  
Media Resource Service Center, Processing

Ideas and submissions can be sent interoffice (Box 68), by electronic mail (newsno), or by fax (212-327-7876).

The Rockefeller University is an equal opportunity/affirmative action employer.





# Drug that caused birth defects born again as potential healer

by Susan Blum

Take a full measure of deadly and debilitating diseases like AIDS, multiple sclerosis, lupus, leprosy, tuberculosis, cancer, and rheumatoid arthritis. Mix well with discoveries about a drug—thalidomide—that has both therapeutic potential and a past as an inducer of horrific birth defects. The result: a recipe for a scientific conundrum, some of whose basic ingredients were prepared by Associate Professor Gilla Kaplan and her colleagues, who continue to study thalidomide today.

In 1991, the Rockefeller researchers discovered that thalidomide—originally prescribed in the 1950s in Germany as a sedative—selectively inhibits tumor necrosis factor, or TNF-alpha. The chemical is a potent immune system cytokine the body produces when mobilized into red alert via innate defense mechanisms or therapeutic interventions against infection. Some TNF-alpha is vital to combat disease, but too much can be harmful or even deadly. Common effects of excessive TNF-alpha include fever, severe weight loss, shock, and profound debilitation.

Kaplan's initial findings came from work on TNF-alpha's action in leprosy. But her subsequent research showed that thalidomide also can quell the cytokine's deleterious effects in infectious diseases such as tuberculosis and AIDS. For example, clinical studies at the Rockefeller University Hospital showed that thalidomide reduces TNF-alpha-induced wasting in patients infected with TB and/or HIV. Test tube experiments also showed that the drug may reduce HIV replication in infected blood cells.

Other studies, some conducted by RU researchers and some performed elsewhere, also show that thalidomide's anti-TNF-alpha action may be therapeutic in rheumatoid arthritis, lupus, and multiple sclerosis. And in a new twist, thalidomide's antiangiogenic properties—its ability to block the growth of new blood vessels—may prove beneficial for disorders as varied as metastatic cancer and degeneration of the eye's macula.

## Catch-22

As word of thalidomide's potential benefits spread, people infected with HIV began circumventing clinical trials, which have strict inclusion criteria. Instead, they imported thalidomide illegally and distributed it in the United States, where the drug has never been approved for use outside clinical studies. This created a Catch-22 situation for both HIV-infected people and for researchers studying

thalidomide. The greater the number of people who received the drug through illegal means, the fewer the number willing to enroll in clinical trials. And without controlled studies, researchers cannot gather the data they need, and a potentially beneficial drug might be made available for legal use.

Now, however, the Food and Drug Administration, AIDS advocates, scientists, and Celgene, the New Jersey-based company that manufactures thalidomide for clinical trials in the United States, are working together to find a way out of this impasse. Their aim: making the drug available on a "compassionate use" basis for those who don't qualify for clinical trials, while still ensuring that patients are monitored and that data about their responses is reliably recorded.

Kaplan has just returned from meetings in Washington where the various players gathered to start laying the groundwork for this new approach. This past summer, the RU researchers played essential roles in establishing both the mentality and the mechanisms necessary for the new strategy. Working in San Francisco with people obtaining thalidomide through "buyers clubs," the scientists helped the AIDS community understand the importance of monitoring patients' responses to thalidomide. They also helped set up the network that will enable physicians to follow their patients when thalidomide becomes available for compassionate use.

## An imperfect drug

While the details of these arrangements are still on the drawing board, one area of agreement already exists: everyone knows that the drug under discussion is an imperfect one. Thalidomide is unstable and its biological activity is short-lived. It has sedative and other side effects. And, of course, it causes terrible birth defects, which is why use of the drug in women of childbearing age is highly regulated.

The ideal solution would be to find analogues—drugs with the same therapeutic effect as thalidomide, but with greater efficiency and fewer or no side effects.

Kaplan and her colleagues are currently working with Celgene scientists to develop such analogues. To begin, they analyzed about a dozen purified thalidomide break-



Associate Professor Gilla Kaplan (left) and her colleagues study the beneficial effects of thalidomide. Kaplan and biomedical fellow Pairote Laochumroonvorapong study the drug's use for leprosy.

down products provided by the German company, Grunenthal, that originally marketed the drug. They then discussed with Celgene how to design compounds with the greatest anti-TNF-alpha activity. Celgene synthesized a large number of molecules and sent them to Kaplan for additional analysis.

So far, visiting scientist Laura Corral has tested some 250 analogues and found three that are very promising, with anti-TNF activities up to 300 times greater than thalidomide's. "Functionally and mechanistically, the analogues' action is the same as thalidomide's," Kaplan reported. Like thalidomide, the analogues inhibit TNF-alpha by hastening degradation of the molecule's messenger RNA. Also like thalidomide, they thwart TNF-alpha activity without dampening other important immune responses.

Moreover, studies in mice, conducted by research associate Andre Moreira, together with Corral and postdoctoral associate Jie Wang, show that the analogues do not sedate. This finding may bode well for concerns about birth defects. "If thalidomide's sedative effects can be separated from its TNF-alpha-suppressive effects, then perhaps its teratogenic effects might be separated, too," Kaplan said.

## Basic research prevails

Compelling as the analogue development work is, the focus of Kaplan's lab remains the study of the regulation of immune-system response, with a special emphasis on the role of TNF-alpha in relation to chronic mycobacterial infections.

For instance, studies of leprosy continue apace in the lab, to learn why—and how—TNF-alpha contributes to immunopathology in this disease. During therapy for leprosy,

some patients develop erythema nodosum leprosum (ENL), a TNF-alpha-mediated inflammatory reaction whose symptoms include fever, painful skin lesions, arthritis, kidney disease, and irreversible nerve damage. ENL affects just a subset of leprosy patients. The researchers, including biomedical fellow Pairote Laochumroonvorapong, want to devise genetic approaches to identifying susceptible populations so that they might be treated prophylactically with thalidomide.

The researchers also study TB meningitis. Predominantly a disease of childhood—particularly in developing countries—TB meningitis is emerging as a significant problem for people infected with HIV. In this condition, a cascade of cytokines mediated by TNF-alpha leads to inflammation. The result is brain swelling, irreversible brain damage, and, sometimes, death.

Just as Rockefeller Associate Professor Elaine Tuomanen showed that the damage of bacterial meningitis can be lessened by giving immune system suppressants along with antibiotics, Kaplan's team, in particular postdoctoral associate Liana Tsenova Berkova, has recently shown that the TNF-alpha-mediated destruction typical of TB meningitis can be halted in animals by administering thalidomide along with antibiotics.

In addition to studying TB in itself, the researchers are exploring the interaction of the slow, ongoing process of HIV infection with infections such as TB. Their studies showed that patients dually infected with HIV and TB have higher levels of both TNF-alpha and HIV than patients infected with HIV alone. "TNF-alpha is a potent trigger for the activation of HIV genes," Kaplan explained, so that TB infection not only causes damage on its own, but hyperactivates the machinery that drives HIV replication. In this, TB may well be a paradigm. "We hypothesize that many opportunistic infections act in the same way," Kaplan said.

A deeper understanding of how opportunistic infections impact on clinical outcome may translate into real benefits for HIV-infected people. "We know that if we can manage patients better, their life expectancy increases and their quality of life improves," Kaplan said. Until such time as a protective vaccine is developed, or a curative drug is found, thalidomide—or safer, more effective analogues—may eventually extend or expand life expectancy to such an extent that, as Kaplan said, "people might actually live with HIV infection as they do with other chronic, potentially lethal diseases."

# Potpourri

Courtesy of the artists



Pianist Valery Kuleshov, silver medallist at the 9th Van Cliburn International Piano Competition, performs works by Bach-Busoni, Saint-Saëns-Liszt, D. Scarlatti, Liszt, and Scriabin at the Tri-Institutional Noon recital today (Oct. 27). The concert, to be held at noon in Caspary Auditorium, is free. All are welcome.

## Celebrating spirits

The 1995 graduate fellows invite all to enjoy a Halloween Party Fri., Oct. 27 at 4:00 P.M. in the Faculty and Students Club. Halloween treats and wine will be served, the free beer hour will be extended, and costumed revelers are welcome. The students thank the Dean's Office for sponsoring the event.

## Friday film

*The Scent of Green Papaya* (France/Vietnam, 1994), directed by Tran Anh Hung, will be shown today (Oct. 27) at 8:00 P.M. in Caspary Auditorium. The film, in French with English subtitles, is free. All are welcome.

## Fall back

Remember to set clocks and watches one hour earlier Sun., Oct. 29. Computers, fax machines, and answering machines should be reset also.

## Sunday reading

The Abigail Adams Smith Museum,

421 East 61th Street, offers a reading of early 19th century writers in a program entitled "Knickerbocker and Leatherstocking: Tales of Irving, Cooper and Poe" Sun., Oct. 29 at 2:00 P.M. The reading is free with museum admission. For further information call 838-6878.

## Ethics course

The Dean's Office is sponsoring a tri-institutional ethics course beginning Tues., Oct. 31. The introductory lecture, which is followed by a panel discussion, will be given by Marguerite Lederberg, attending psychiatrist at Memorial Sloan-Kettering Cancer Center. The other lectures in this series are:

- Tues., Nov. 14: "Science as a Social Enterprise" Carl Nathan, professor of medicine, Cornell University Medical College;
- Tues., Nov. 21: "Ethics of Data Management" Peter Model, professor, RU;

•Tues., Nov. 28: "Ethics of the Use of Living Research Subjects" Joseph Fins, assistant professor of medicine, Cornell University Medical College.

The lectures, held in Cornell's Uris Auditorium, will be followed by discussions. For further information contact Marguerite Mangin, x8086.

## Clinical Research Seminar

Martin Lipkin, a member of Memorial Sloan-Kettering Cancer Center and head of the Irving Weinstein Laboratory for Gastrointestinal Cancer Prevention, will discuss "Chemoprevention of Colon Cancer" Wed., Nov. 1 at noon in Nurses Residence 110B.

## Ribbon cutting

*The Roundabout*, Alice Aycock's sculpture at the East 60th Street Pavilion, will be formally dedicated at a ribbon-cutting ceremony Mon., Nov. 6 at 11:00 A.M. at the pavilion.

## Library tutorials

The library offers personal one-on-one tutorials for the MEDLINE and Current Contents databases. For fur-

## Health office offers free flu shots

The annual influenza vaccination program at Rockefeller begins Wed., Nov. 1. All adults on campus may obtain free flu shots in the Employee Health Office, Hospital 118. No appointment is necessary.

Strains in the vaccine are A/Texas/36/91 (H1N1), A/Johannesburg/33/94 (H3N2), and B/Harbin/07/94. Because influenza viruses change frequently, the shot does not guarantee immunity, but for those who catch one of the expected viruses, it minimizes symptoms.

Questions may be addressed to Mary Brust or Aurea Tuason in the health office, x8414.

ther information contact David Man, x8907 or e-mail mand.

## Pool tournament

The Faculty and Students Club has posted the schedule of players for the singles pool tournament. The first round must be completed by Fri., Nov. 10.



They were raking it in at the Children's School this week, aided by Sarah O'Leary, grounds worker.

# Cohen

(continued from page 1)

ural constraints, which are emphasized by ecologists, and human choices, which are emphasized by social scientists—even such apparently trivial choices as wearing cotton or polyester and building parks or parking lots.

Cohen received doctoral degrees from Harvard University in applied mathematics (1970) and population sciences and tropical public health (1973). He joined the Harvard faculty in 1971 as an assistant professor in the Department of Biology

and a lecturer in population sciences at the School of Public Health. He came to Rockefeller in 1975 as professor and head of laboratory.

Cohen has received many honors and awards. He was a fellow of the John D. and Catherine T. MacArthur Foundation and the John Simon Guggenheim Memorial Foundation. In 1983 he was elected a member of the American Association for the Advancement of Science. He received the 1972 Mercer Award of

the Ecological Society of America, the 1992 Mindel C. Sheps Award of the Population Association of America, and the 1994 Distinguished Ecologist Award from the INTECOL Statistical Ecology Group. From 1989 to 1990 he was Director's Visitor at the Institute for Advanced Study in Princeton.

The lecture will be held at 3:45 P.M. in Caspary Auditorium and preceded by tea at 3:15 P.M. in Abby Aldrich Rockefeller Lounge. All are welcome.

# Hanafusa

(continued from page 1)

the American Association for the Advancement of Science, and the American Association of Cancer Research. He serves on the editorial boards of the *Journal of Virology* and *Molecular Cellular Biology*.

He is married to the former Teruko Inoue, a senior research associate at RU. Other recipients of the Order of Culture are novelist Shusaku Endo, lacquer artist Tadashi Saji, law professor Shigemitsu Dando, and Shiro Masuda, professor of western economy.