# Current Comments

## A Tribute to Hilary Koprowski: Scientist, Musician, and Friend

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In a previous essay describing scientific places of interest in Philadelphia,[1] I mentioned the Wistar Institute, located on the campus of the University of Pennsylvania just a few blocks from ISI®. Wistar is the oldest biomedical research institute in the US. Although it has some cooperative arrangements with the university, Wistar is a completely independent organization.

While this is the year of the Philadelphia tercentennial, in May we also celebrated an important silver jubilee—the anniversary of the arrival of Wistar's dynamic director, Hilary Koprowski. The occasion reminded me that a tribute to him was long overdue. During the 25 years of Koprowski's leadership, Wistar has become one of the foremost research centers in the world. And as this essay will demonstrate, he is not only a dedicated and prolific scientist, but a talented musician as well.

Joshua Lederberg introduced me to Koprowski in 1958, the year Lederberg won the Nobel prize for his work on the genetics of bacteria. It is interesting to note that we also celebrated the twenty-fifth anniversary of *Current Contents*® (*CC*®) this year.[2] So at the same time I was launching *CC/Life Sciences* and the organization that would become ISI, Koprowski was beginning to assemble his new organization of top researchers at Wistar. Thus, we shared a common experience in "scientific entrepreneurship."

From the beginning, Koprowski was very supportive of ISI's effort to make information retrieval more rapid and effective—first as a user, then, since 1964, as a member of the editorial advisory board of *Science Citation Index*® (*SCI*®). In 1968 he became a member of our Board of Directors.

Koprowski is unquestionably one of the outstanding biomedical scientists of our time. Space will not permit a complete and detailed account of his accomplishments. He was the first to develop an oral polio vaccine and to administer it to humans.[3] With Tadeusz Wiktor and other co-workers at Wistar, he developed a new rabies vaccine that is more effective and less painful than the traditional Pasteur technique.[4,5] This discovery alone would establish him as a pioneer. But Koprowski has also studied the etiology of multiple sclerosis and of cancer. And he has pioneered the development of monoclonal antibodies with specificities for viruses and human cancers.

Koprowski was born in 1916 in Poland. At age 12, he entered the Warsaw Conservatory of Music to study piano. He continued to study music part-time at the conservatory through his high school years and even while in medical school at the University of Warsaw. Two years prior to his graduation from medical school, Koprowski worked as a research assistant in the department of experimental pathology. It was also in medical school that he met his wife, Irena Grasberg. They were married in 1938. She is now professor of pathology at Temple University, Phila-

*Hilary Koprowski*

delphia. The Koprowskis have two sons, Claude and Christopher. Claude is now a physician specializing in emergency medicine in Florida, but I knew him as an excellent journalist before he decided to study medicine. Christopher is now a resident in neurology at the Hospital of the University of Pennsylvania. He is also enrolled in the graduate program at the university's Wharton School.

In 1939, Koprowski received his medical degree from the University of Warsaw. When World War II broke out, he left Poland for Italy. During the brief period before Italy entered the war, Koprowski volunteered as a physician for the Polish draft board-in-exile. Through this organization, Polish citizens living outside Poland could enlist in the armies of the Allied Forces. Koprowski also attended the Conservatorio di Musica Santa Cecilia in Rome, where he continued his music studies from 1939 to 1940.

In June 1940, Koprowski left Italy and resettled in Brazil. An opportunity to pursue biomedical research in that country arose by chance. On the streets of Rio de Janeiro, he met Luty Kosobudski, a physician who had attended Koprowski's high school in Poland. Kosobudski had returned to Brazil where he was born. He informed Koprowski that the Rockefeller Foundation's Yellow Fever Research Service in Brazil was enlisting people to work in their labs. Before long, Koprowski was performing research in yellow fever and neurotropic viruses. His work was supported jointly by the Rockefeller Foundation and the Ministry of Education of Brazil.

It was during this period that Koprowski finally decided on a career in science rather than music. He explained this decision to me in his office. "I gave a few piano concerts when I arrived in Brazil, and realized that I did not have the skill and education to go to the top of the profession. I did like to give piano lessons, but never considered that as a permanent career."[6] But Koprowski never abandoned music. He still plays the piano almost every day. Each year at Christmas, he gives a concert for the Wistar staff. He brings sheet music along on his frequent business trips, and searches out a piano whenever he finds time. I admire his discipline and dedication. I found it difficult to do the same with my saxophone.

Having decided on a scientific career, Koprowski left Brazil in 1944 to become a research associate at American Cyanamid's Lederle Laboratories, Pearl River, New York. Two years later, he was appointed assistant director of Lederle's Viral and Rickettsial Research Program, a post he held until coming to Wistar as director and institute professor. At the same time, he was named Wistar professor of research medicine, and professor of microbiology at the University of Pennsylvania—positions that he holds to this day.

Oddly enough, what attracted Koprowski to Wistar was that venerable institute's lack of activity. Wistar was founded in 1892 in memory of surgeon Caspar Wistar and his colleague, William E. Horner. At first, the institute was primarily devoted to neuroanatomy, and later to studies in neurology, comparative anatomy, and embryology. But when Koprowski arrived, the institute was, as he puts it, "an empty shell."[6] In a

situation that might have led others to despair, Koprowski saw unlimited possibilities. "That was the great attraction," he told me, "to bring in the people you wanted and to build something from scratch."[6]

Under Koprowski's direction, more than 100 scientists have joined Wistar. Koprowski attributes his success in attracting talented people to his unique plan for Wistar: "My idea was that it would be a decentralized institution, with the director playing the role of scientist, rather than administrator. This gave the other scientists freedom to work on whatever they wished."[6] In spite of their independence, Wistar scientists collaborate closely with each other. Many disciplines are represented on each research project. However, the decentralized structure has made it easier for Koprowski to carry his own full research load. His extensive bibliography reflects this. He has published more than 500 papers, about 400 of these during his 25 years at Wistar.

Koprowski's outstanding contributions have earned him memberships in the US National Academy of Sciences, the American Academy of Arts and Sciences, and the Yugoslav Academy of Sciences and Arts. He is a fellow of the College of Physicians of Philadelphia, and the New York Academies of Medicine and Sciences. He currently serves as a consultant to the World Health Organization and the Pan American Health Organization. Koprowski has been the Alexander von Humboldt professor at the Max Planck Institute, Martinsried, Bavaria, and a Fulbright Scholar studying ethology with Konrad Lorenz at the Max Planck Institute for Behavioral Physiology, Seewiesen. This listing of honors and affiliations is by no means exhaustive.

Peer recognition in the form of academy memberships usually correlates with citation frequency. Koprowski is no exception to this rule. As a primary author, he was cited nearly 2,200 times in *SCI* from 1961 to 1981. He appeared on our list of the 1,000 most-cited authors—including coauthors—from 1965 to 1978.[7] The 4,200 citations he received during this period place him among the top quarter of this distinguished group. He was also on our list of the 300 most-cited authors from 1961 to 1976.[8]

Koprowski published his most-cited paper in 1962. That article, entitled "Transformation of cultures of human tissue infected with simian virus SV40," has been cited in over 270 papers since its publication. A bibliography of Koprowski's most-cited publications appears in Table 1.

Another very influential paper by Koprowski and colleagues described how the chromosomes of SV40 become activated in host cells to produce a complete virus. That paper has received nearly 250 citations since its publication in 1967.

Koprowski continues to perform research at the forefront of biomedical research. He and his colleagues are investigating numerous types of cancer, chronic diseases of the central nervous system, rabies, and other viral infections. When we checked our *ISI/BIOMED*™ online data base, we found that Koprowski is the author of one or more papers in the 26 research front specialties listed in Table 2.

Some of Koprowski's most recent and exciting work involves monoclonal antibodies, which are highly specific disease fighters secreted by hybrid cells produced in the laboratory. These hybrids result from the fusion of a tumor cell and a healthy spleen cell (B-lymphocyte) that has been immunized against a given disease. The hybrids, called lymphocyte hybridomas, have both the spleen cell's disease-fighting antibody and the tumor cell's capacity for indefinite survival. Monoclonal antibodies secreted from lymphocyte hybridomas are now produced in large amounts, and promise to revolutionize the treatment of a variety of diseases, from breast cancer to rabies. Monoclonal antibodies are also useful for mapping the genes of defective chromosomes suspected of causing inherited diseases.

**Table 1:** Most-cited articles by Hilary Koprowski.

| Total Citations 1962-81 | Bibliographic Data |
|---|---|
| 271 | **Koprowski H, Ponten J A, Jensen F, Ravdin R G, Moorhead P & Saksela E.** Transformation of cultures of human tissue infected with simian virus SV40. *J. Cell. Comp. Physiol.* 59:281-92, 1962. |
| 249 | **Koprowski H, Jensen F C & Steplewski Z.** Activation of production of infectious tumor virus SV40 in heterokaryon cultures. *Proc. Nat. Acad. Sci. US* 58:127-33, 1967. |
| 173 | **Koprowski H & Fernandes M V.** Autosensitization reaction *in vitro*. *J. Exp. Med.* 116:467-76, 1962. |
| 153 | **Girardi A J, Jensen F C & Koprowski H.** SV40-induced transformation of human diploid cells: crisis and recovery. *J. Cell. Comp. Physiol.* 65:69-83, 1965. |
| 121 | **Croce C M, Girardi A J & Koprowski H.** Assignment of the T-antigen gene of simian virus 40 to human chromosome C-7. *Proc. Nat. Acad. Sci. US* 70:3617-20, 1973. |
| 120 | **Barbanti-Brodano G, Oyanagi S, Katz M & Koprowski H.** Presence of two different viral agents in the brain cells of patients with subacute sclerosing panencephalitis. *Proc. Soc. Exp. Biol. Med.* 134:230-6, 1970. |
| 108 | **Croce C M, Koprowski H & Eagle H.** Effect of environmental pH on the efficiency of cellular hybridization. *Proc. Nat. Acad. Sci. US* 69:1953-6, 1972. |
| 102 | **Oyanagi S, ter Meulen V, Katz M & Koprowski H.** Comparison of subacute sclerosing panencephalitis and measles virus: an electron microscope study. *J. Virol.* 7:176-87, 1971. |
| 99 | **Croce C M, Sawicki W, Kritchevsky D & Koprowski H.** Induction of homokaryocyte, heterokaryocyte and hybrid formation by lysolecithin. *Exp. Cell Res.* 67:427-35, 1971. |
| 93 | **Sokol F, Kuwert E, Wiktor T J, Hummeler K & Koprowski H.** Purification of rabies virus grown in tissue culture. *J. Virol.* 2:836-49, 1968. |
| 80 | **Katz M, Oyanagi S & Koprowski H.** Subacute sclerosing panencephalitis: structures resembling myxovirus nucleocapsids in cells cultured from brains. *Nature* 222:888-90, 1969. |
| 80 | **Croce C M, Aden D & Koprowski H.** Somatic cell hybrids between mouse peritoneal macrophages and simian-virus-40-transformed human cells. II. Presence of human chromosome 7 carrying simian virus 40 genome in cells of tumors induced by hybrid cells. *Proc. Nat. Acad. Sci. US* 72:1397-400, 1975. |
| 74 | **Siniscalco M, Klinger H P, Eagle H, Koprowski H, Fujimoto W Y & Seegmiller J E.** Evidence for intergenic complementation in hybrid cells derived from two human diploid strains each carrying an X-linked mutation. *Proc. Nat. Acad. Sci. US* 62:793-9, 1969. |
| 73 | **Croce C M & Koprowski H.** Somatic cell hybrids between mouse peritoneal macrophages and SV40-transformed human cells. I. Positive control of the transformed phenotype by the human chromosome 7 carrying the SV40 genome. *J. Exp. Med.* 140:1221-9, 1974. |

In a 1977 article published in *Proceedings of the National Academy of Sciences of the USA* (*PNAS*), Koprowski, Walter Gerhard, and Carlo M. Croce reported the production of the first useful monoclonal antibodies.[9] These were secreted by mouse hybridomas to counter influenza virus. That article was cited 92 times from 1977 to 1981. Another *PNAS* paper on monoclonal antibodies defining antigens of human cancers[10] received 92 citations in only three years, 1979-1981. This paper is one of the core documents for the 1981 *ISI/BIOMED* research front specialty, "Monoclonal Antibodies." In a 1980 paper in *Nature*, Croce, Koprowski, and other Wistar researchers reported another breakthrough: the development of human hybridomas that could be bred and "cloned" without limit.[11] Prior to this discovery, human spleen cells failed to survive in culture, and cells from rodents were used to produce hybridomas. This paper has already received 24 citations. Since antibodies from human hybridomas are more effective in fighting human illnesses,

**Table 2:** 1980 *ISI/BIOMED*™ research front specialties in which the work of Hilary Koprowski appears.

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|---|---|
| 80-2536 | Analysis of CSF antibodies in multiple-sclerosis |
| 80-1460 | Carcinoembryonic antigen-release from human colon-carcinoma |
| 80-0770 | Cell-growth in serum-free medium |
| 80-2788 | Characterization of monoclonal antibodies to human melanoma-associated antigens |
| 80-2175 | CSF IGG profiles as diagnostic techniques in multiple-sclerosis |
| 80-0395 | Deoxynucleotidyl-transferase activity and characteristics of blast-cells in leukemia |
| 80-2015 | Epstein-Barr virus-associated antibodies in nasopharyngeal-carcinoma |
| 80-0341 | Expression, regulation, movement and recombination of transformed cell-lines |
| 80-0456 | Globin M-RNA precursor |
| 80-1035 | Glycoprotein-synthesis and gene-expression of herpes simplex virus genome |
| 80-0413 | Herpes simplex virus infections of nervous system |
| 80-0131 | HLA-DR antigens |
| 80-0765 | Host virus interactions during transformation |
| 80-1428 | Interferon-mediated control of natural killer-cell activity in tumor cells |
| 80-0641 | Immunochemistry of Langerhans-cells |
| 80-2016 | Immunological cytotoxicity induced by Epstein-Barr virus infection |
| 80-0223 | Immuno-response studies in multiple-sclerosis |
| 80-2024 | Monoclonal antibodies to human tumor antigens |
| 80-1766 | Monoclonal antibody inhibition of cross-reactive cytotoxic T-cells |
| 80-1436 | Organization of Epstein-Barr virus DNA |
| 80-2107 | Production of drug antibody-conjugates in treatment of tumors |
| 80-1187 | Protein-synthesis in diphtheria toxin-resistant-cells |
| 80-2549 | Purification and cytotoxicity of ricins from ricinus-communis |
| 80-0763 | Role of glycoproteins and protein-protein-interactions in viral pathogenesis |
| 80-2099 | Somatosensory evoked potentials and central afferent-conduction analysis in multiple-sclerosis |
| 80-1629 | Suppression-mechanisms of T-cell membrane-bound FC-fragments in lymphoproliferative disorders |

there is little doubt that the impact of this paper on future research will become increasingly evident.

Although Koprowski is generally optimistic about the future of scientific research, he is concerned that young people are losing interest in science. "The problem of the scientific community today is that young people are not attracted to careers in science. Perhaps the funding cutbacks make them afraid they won't find jobs in science. Or maybe science is losing the glamour it once had."[6]

Koprowski believes the solution lies in placing greater emphasis on gifted children, a topic I have discussed earlier.[12] As Koprowski puts it, "The United States has an enormous, though decreasing, amount of money for disadvantaged children, crippled children, and mentally deficient children. But there's very little for really talented youngsters. If you pick out the excellent people, and from the very beginning cultivate an elite of magnificent scientists, this will attract others. Unfortunately, we are not doing this."[6] Koprowski feels that the way in which schools in the US are currently run only stifles the curiosity of bright students and forces them to conform to a level of mediocrity, instead of placing them on the "road to excellence."[6]

Koprowski has also expressed the concern that students specialize too early in life, and forfeit the benefits of a broad education.[13] His emphasis on the importance of a broad, humanistic education is reflected in his view of science as a "creative art."[6] Not surprisingly, he laments the division between the arts and sciences in modern society, and feels that scientists have much in common with artists. As he recently stated in an interview: "A well-devised, well-conceived experiment is as difficult to construct as a sonata...and the results one gets when an experiment works are

as satisfying as the feeling one gets [composing] music."[14]

Through his undying love for music, and his outstanding accomplishments in science, Koprowski has succeeded in bridging the two cultures. In spite of the present dearth of attention to gifted children, his example can inspire future generations of scientists. It can make even the most conservative supporters of education realize the benefit society reaps by supporting genius at an early age.

In closing I cannot fail to comment on the personality of the man, which only barely comes through in a photograph. Whenever he walks into our board meetings, one senses that the room lights up. He has a marvelous sense of humor. You are always aware of his impatience with verbosity, and his ability to catch the most important details. In a business or scientific discussion you sense his need to be succinct, yet at the dinner table he is charming and relaxed.

It has been a unique privilege for me to enjoy his friendship for so many years. It is a great pleasure to acknowledge this publicly for the first time. In particular, without his support, ISI's new building would not be a reality. The same can be said about the new ISI Caring Center for Children and Parents now under construction. I look forward to his participation in the opening ceremonies in September 1982.

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## REFERENCES


1. **Garfield E.** You're invited to historic Philadelphia for the tercentennial. *Current Contents* (1):5-13, 4 January 1982.
2. ----------, On the 25th anniversary of *Current Contents/Life Sciences* we look forward to the electronic online microcomputing era. *Current Contents* (4):5-11, 25 January 1982.
3. **Koprowski H, Jervis G A & Norton T W.** Immune responses in human volunteers upon oral administration of a rodent-adapted strain of poliomyelitis virus. *Amer. J. Hygiene* 55:108-26, 1952.
4. **Wiktor T J & Koprowski H.** Successful immunization of primates with rabies vaccine prepared in human diploid cell strain WI-38. *Proc. Soc. Exp. Biol. Med.* 118:1069-73, 1965.
5. **Sikes R K, Cleary W F, Koprowski H, Wiktor T J & Kaplan M M.** Effective protection of monkeys against death from street virus by post-exposure administration of tissue-culture rabies vaccine. *Bull. WHO* 45:1-11, 1971.
6. **Koprowski H.** Personal communication. 8 January 1982.
7. **Garfield E.** The 1,000 contemporary scientists most-cited 1965-1978. Part 1. The basic list and introduction. *Current Contents* (41):5-14, 12 October 1981.
8. ----------, The 300 most-cited authors, 1961-1976, including co-authors at last. 1. How the names were selected. *Essays of an information scientist.* Philadelphia: ISI Press, 1980. Vol. 3, p. 538-50. (Reprinted from: *Current Contents* (28):5-17, 10 July 1978.)
9. **Koprowski H, Gerhard W & Croce C M.** Production of antibodies against influenza virus by somatic cell hybrids between mouse myeloma and primed spleen cells. *Proc. Nat. Acad. Sci. US* 74:2985-8, 1977.
10. **Koprowski H, Steplewski Z, Herlyn D & Herlyn M.** Study of antibodies against human melanoma produced by somatic cell hybrids. *Proc. Nat. Acad. Sci. US* 75:3405-9, 1978.
11. **Croce C M, Linnenbach A, Hall W, Steplewski Z & Koprowski H.** Production of human hybridomas secreting antibodies to measles virus. *Nature* 288:488-9, 1980.
12. **Garfield E.** Will a bright mind make its own way? *Essays of an information scientist.* Philadelphia: ISI Press, 1981. Vol. 4, p. 713-23. (Reprinted from: *Current Contents* (51):5-15, 22 December 1980.)
13. **Knight H.** "Don't make gods of scientists!" *Phila. Bull. Mag.* 9 March 1980, p. 4-6.
14. **Lawrence S V.** Wistar: the spirit of free inquiry. *Forum Med.* 3:658-61, 1980.