**A giant scientific breakthrough that turned out to be a fraud.**

(by Volker M. Vogt)

 “*Scandal in the laboratory”*. That was the headline of one of many news articles dealing with the bizarre case of a graduate student in Ef Racker’s lab in 1980-81. It ended up as one of the most spectacular cases of scientific fraud in the second half of the 20th century.

 Mark Spector came to Ef’s lab in January 1980. He had earned an MS at the University of Cincinnati with one of Ef’s former associates, had already been first author on an important paper on photosynthesis [1], and had been touted as a budding super-star. The graduate admissions committee made an exception by admitting him to the BMCB program at midyear, January 1980, instead of for the fall, and by allowing him to become a student immediately in the Racker lab, without requiring any rotations in other labs or any teaching experience. Ef had a hypothesis that the well-known, high glycolysis rate in cancer cells was due to an “inefficient” Na-K pump (also known as the Na-K ATPase), which maintains the proper balance of ions in cells, pumping K+ into the cell and Na+ out. He further hypothesized that the inefficiency of this ion pump played a causal role in cancer. Ef gave to Spector as a thesis project the molecular characterization of the Na-K pump from mouse ascites cells, a type of cancer cell that can be grown easily in large quantities and therefore was suitable for biochemical studies.

 In his first few months as a grad student, Mark speedily purified the ATPase, and then proceeded to show that it indeed was inefficient, i.e. used more ATP to pump the same number of ions across the plasma membrane than did the same enzyme from normal cells. On the heels of that discovery came another, that the ascites cell enzyme was phosphorylated by a protein kinase activity present in the tumor cells. Moreover, phosphorylation made the ATPase inefficient, establishing a link between phosphorylation and the enzymatic properties of the ATPase. A manuscript reporting these findings was submitted to the Journal of Biological Chemistry (JBC) in June of 1980, i.e. about one half year after Spector came to Cornell, and was published in September of that year [2].

 In the following few months the story was elaborated further with the emergence of a “kinase cascade”, which was described in a JBC article submitted in December1980 and published in May 1981 [3]. Using an assay with the purified ATPase as a substrate (or “bait”) and radioactive 32P-ATP as a phosphate donor, Spector searched in ascites cell extracts for the enzyme responsible for the phosphorylation. He found and purified this enzyme, by definition a protein kinase, naming it PKM. PKM then also turned out to be phosphorylated, with the attachment of the phosphate serving to activate (“turn on”) its kinase activity. Using the same experimental strategy but with de-phosphorylated PKM as a substrate, Spector then purified a second kinase, named PKS. With this iterative procedure of using one protein as substrate to find, purify, and characterize the kinase that phosphorylated it, he came up with the following scheme: PKL -> PKS -> PKM -> ATPase. One protein kinase phosphorylated the next, thereby activating it, with the cascade finally terminating at the ATPase, rendering that enzyme inefficient as a Na-K pump. The date when the second JBC paper was submitted implies that all of this work was completed in less than a year after Spector’s arrival at Cornell, in hindsight a feat unimaginable even for the most gifted and lucky biochemist, let alone a beginning grad student.

 Further elaborations of the kinase cascade followed in the spring of 1981. Spector claimed to show that the phosphorylation of the ATPase and of the three kinases took place on the amino acid tyrosine. For more than a decade it had been known that protein phosphorylation (i.e. covalent addition of a phosphate group to an amino acid) could occur on the amino acids serine or threonine, and that this event in some cases caused a change (“regulation”) in the properties of the target protein. However, less than two years before Spector came to Cornell, phosphorylation of a third amino acid, tyrosine, had been discovered in studies of a cancer-inducing protein encoded by a mouse DNA tumor virus called polyoma [4]. Immediately following that discovery, several leading labs in the US showed that phosphorylation of tyrosine frequently is a signal used by normal cells to regulate proliferation, a generalization that still holds in the 21st century. For example, the plasma membrane receptors for small polypeptide growth hormones like epidermal growth factor (EGF), platelet-derived growth factor (PDGF), and insulin all are tyrosine-specific protein kinases. Similarly and also just preceding Spector’s ATPase work, the oncogenic protein encoded by the chicken retrovirus Rous sarcoma virus (RSV) was itself shown to be a tyrosine kinase [5]. Thus, in a short time the emerging molecular biology of cancer seemed to have converged on a central role for tyrosine phosphorylation. As a consequence, Spector’s report that his kinases and the Na-K ATPase all were phosphorylated on tyrosine, and that in each case this phosphorylation served a regulatory function, immediately was taken as a powerful suggestion that the ATPase played a critical role in cancer, apparently vindicating Racker’s hypothesis.

 By late spring of 1981 Spector had come up with a final version of the kinase cascade shown in **Figure 1**, which is taken from the May 1981 cover of the abstract booklet for the annual international meeting on RNA tumor viruses (later re-named retroviruses) at Cold Spring Harbor, NY. At that meeting Spector was allowed an unprecedented 45 min (rather than the usual 15 min) to orally present the results of his research. The cascade now included a fourth kinase, PKL. In addition, Spector claimed that some of the kinases could be phosphorylated by, and thereby activated by, retroviral protein kinases (diamonds at left in Figure 1) that had just in the past two years been implicated as the causative agents for the cancer-inducing ability of several retroviruses that infect chickens, mice, or rats. *[footnote 1].*

 At that time, a generalization emerging from many laboratories was that for many cancer-causing animal viruses, the viral genes responsible for oncogenic transformation were originally picked up by the virus from host cells. These genes, called “proto-oncogenes” when they were in normal cells, acquired mutations once they became part of the viral genome. The resulting mutant forms of the proteins encoded by the genes were deranged in function, causing the cell to lose growth control when infected by the virus. The paradigm for this generalization was RSV and the viral v-Src protein, the founding member of cancer-inducing tyrosine kinases and the first viral protein identified as originating in the host cell (later leading to a Nobel prize for Michael Bishop and Harold Varmus).

 A final key element of this last version of the kinase cascade was the claim that PKL was identical to the cellular c-Src protein, i.e. was identical to the progenitor of the RSV v-Src protein encoded by the virus. Evidence for this supposed identity included immunological cross-reactivity and peptide mapping. These results were described in a paper submitted for publication in the journal Cell in March 1981 and published a few months later [6].

 The audience at the retrovirus meeting in May 1981 was spell-bound by the story that Spector unfolded of his characterization of four tyrosine-specific protein kinases, functionally linked in a “cascade” that directly or indirectly was linked to known viral kinases implicated in tumorigenesis. Nevertheless, some in the audience were skeptical. They doubted that these accomplishments were humanly possible in the short one and a half years Spector had been at Cornell. One post doc in a famous lab said openly that Spector’s phospho-amino acid analyses clearly were faked, because the radioactive “spots” visible on the two-dimensional plate on which the amino acids were separated from each other were far too small. But Spector obviously was highly intelligent and really understood the biology and biochemistry of his and others’ work. And he had an answer for everything when challenged. Also, the kinase cascade incarnated the simple principles that cancer researchers for years had hoped would underlie this disease. For these and other reasons, most of the research community remained credulous. Foremost among them was Spector’s mentor Ef Racker, who staunchly defended him and his work.

 Volker Vogt was an Assistant Professor with a lab upstairs from Ef Racker’s lab. The two lab heads did not communicate much, since the main focus of the Vogt lab was quite different, retrovirus assembly. The question his lab addressed, using mainly the avian RSV virus as a model system, was how viral proteins and cellular membranes and the viral RNA genome come together to make an infectious virus particle. But in the late 1970s and early 1980s the molecular basis of cancer induction by viruses was a hot topic, and thus Volker always heard the latest news at the virology meetings he attended. In addition, he taught an advanced course on cell proliferation and oncogenic viruses. A grad student in the Vogt lab, Blake Pepinsky, knew the Racker lab since he had done a rotation project there, and starting in spring 1980 he and Mark Spector often socialized, since both liked to work at night. Blake and Volker often discussed with Mark the latest research papers or meeting reports on viral oncogenesis, and also discussed Spector’s emerging data.

 The threads in Spector’s kinase cascade began to unravel by spring 1981. But already long before then, problems with Spector’s claims had surfaced, most becoming clear only in hindsight. For example, in the spring of 1980 Spector learned from Pepinsky the technique of immune precipitation, which was used commonly in the Vogt lab, and which subsequently figured prominently in Spector’s subsequent claims. In this technique, a purified protein is injected into a rabbit to generate antibodies, and then the antibodies, being highly specific, are used to capture the protein of interest from a crude extract of cultured cells that had been labeled with a radioactive amino acid. The resulting “immune precipitate” is then dissolved in a detergent called SDS, and the radioactive proteins are visualized by polyacrylamide slab gel electrophoresis (SDS PAGE) followed by autoradiography. If the protein of interest is expressed in the cells, and if the antibody works as expected, a radioactive “band,” detected on a photographic film, appears on the gel. Spector claimed to have made a rabbit antiserum to the Na-K ATPase, and he produced many films that showed impressively clean radioactive bands that he claimed to be the two ATPase polypeptides.

 But other people, both in the Racker lab and including Blake Pepinsky, could not repeat these results unless Spector had some role in the experiments. In the late spring of 1980, i.e. less than a half year after Spector arrived at Cornell, Volker took it on himself to try to figure out why the immune precipitations were not reproducible, requesting and receiving from Mark samples of the antiserum to the Na-K ATPase as well as a test tube labeled “Na-K ATPase”. After two months of intense experiments trying to track down what “inhibitor” substance might be preventing the immune precipitation from working, he eventually figured out that the protein labeled “ATPase” in the test tube from Mark in fact was bovine serum albumin (BSA, a protein one can purchase inexpensively), and that the rabbit antiserum labeled “anti-ATPase” in fact was anti-BSA. Vogt was incensed. How could anyone inject a rabbit with the wrong protein, and then also label a test tube incorrectly? But Spector simply apologized and ascribed this to a clerical “mix-up” due to mis-labeling of tubes. Similar “mix-ups” involving other people were documented after the fact over the following nine months. While initially deciding to wash his hands of everything to do with Spector, by late fall 1980 Volker was again seduced by the spectacular results that this highly intelligent and apparently experimentally gifted student generated.

 A similar “mix-up” in late spring 1981 involved the lab of Ray Erikson, who at that time was in Colorado. This incident became rather widely known via the rumor mill, causing more researchers to doubt Spector’s claims. When researchers in different laboratories independently discover what may be the same protein, they routinely trade reagents to help establish or rule out this possible identity. Reagents include the protein itself, if it is available in purified form, and antibodies made against the protein. When Spector claimed that PKL was identical to c-Src, the cellular version of the Rous sarcoma virus v-Src protein, which by that time had been established as a tyrosine-specific protein kinase, it was logical to trade reagents with a lab studying RSV and v-Src. Accordingly, Erikson’s lab sent the Racker lab a sample of antiserum that they had made to the RSV v-Src protein, and Spector was supposed to reciprocate with his anti-PKL serum. He did go through the motions of this reagent exchange. But in fact what he sent back to Erikson was a portion of the same antiserum he had received from them. The Erikson lab was able to identify it as their own antiserum because of the particular way they had generated the antiserum in the first place (using the RSV virus to induce a rabbit tumor, with the rabbit then also making antibodies to the viral structural proteins). When confronted, Spector claimed, as he did repeatedly, that he had made a simple clerical error, sending the wrong tube. In hindsight it seems incredible that all of these supposed “mix-ups”, which involved people in the Racker lab, the Vogt lab, and also several labs at other universities, didn’t trigger more disbelief.

 What was missing in early summer 1981 was a model to explain all the clean and abundant data Spector had apparently generated. For example, he had what seemed to be reams of autoradiographs—photographic films with black bands corresponding to the radioactive kinase and ATPase proteins—displayed by SDS PAGE. These radioactive proteins were supposedly tagged with either of two different radioactive isotopes. In one case, cells were fed 35S-methionine (an amino acid found in all proteins), resulting in labeling of all cellular proteins. In the other case, the cells were fed a different isotope and chemical, 32P-phosphate, which tags only those proteins that are phosphorylated. Spector routinely used both isotopes, as did many labs. For example, he sometimes labeled parallel cultures of normal and cancer cells, made crude extracts of both, collected each of the four kinases with his supposedly specific rabbit antisera, and then displayed the radioactive bands corresponding to the specific proteins on a film that had been laid on the SDS polyacrylamide slab gel. The typical result was that both normal and cancer cells showed an 35S-labeled band corresponding to the kinase, but that only the cancer cells showed that protein in the 32P-labeled cells, implying that the phosphorylation but not the synthesis of the protein was cancer cell-specific. Two examples of autoradiographs in Spector’s notebooks are shown in **Figures 2** and **3**.

 In hindsight, the obvious red flag was that the radioactive bands, corresponding to the kinases or the ATPase, were far too prominent. The kinases were claimed to be minor proteins, corresponding to less than 1% of all cell proteins, and so any research scientist routinely using this technique would consider the very black bands on autoradiograms like that in Figure 2 to be extraordinary, bordering on the impossible. But there they were anyway, spectacularly clear and apparently leading to unambiguous conclusions.

 The kinase cascade collapsed in summer 1981, only a month after the world-wide publicity from the Cold Spring Harbor meeting and from the various talks that Racker had given on Spector’s work over the past year. In fact, the cascade was totally faked. None of the kinases ever existed, nor did the purified ATPase that Spector claimed to have prepared.

By late spring 1981 Volker was one of the numerous people who were privately skeptical about Spector, although Volker defended the scientific results publically, for example at the Cold Spring Harbor meeting in May. Everyone in the Vogt lab knew that Spector made up stories about his private life—sometimes outrageous stories—and this was a frequent topic of conversation in the lab in spring 1981. Everyone also knew that not a single person either in the Racker lab, the Vogt lab, or in any lab outside of Cornell had been able to independently repeat Spector’s key scientific findings. However, this skepticism about Spector as a person surprisingly did not lead to any direct challenge of the authenticity of his scientific data, probably because of the lack of any hypothesis that could explain the high quality “data” in the form of autoradiographic films with intense dark “bands” supposedly corresponding to the ATPase and the four kinases that he claimed to be studying.

 In one of Spector’s occasional thesis committee meetings, some of which Volker attended, Spector was pestered to come up with more quantitative data on the phospho-amino acids in the kinases, when these were isolated from cells growing under different conditions, for example. He eventually did that, producing several pages of numbers. Volker was suspicious that so many measurements could have been made in such a short time. In addition, he wanted to learn the technique of phosphoamino acid analysis for possible use later in his lab. This technique involves dissolving and hydrolyzing a 32P-labeled protein in hydrochloric acid, and then separating and identifying the radioactive amino acids (serine, threonine, or tyrosine) by two dimensional chromatography and electrophoresis. Spector’s dried SDS polyacrylamide gels seemed a good place to start—they could provide radioactive protein, and the gels were no longer of use to Spector once the photographic film corresponding to each had been developed. Also, Volker figured that this exercise might be a good way to check on the accuracy of Spector’s claims about tyrosine phosphorylation. Mark promised to give him the gels, but always found an excuse not to do so. However, Blake knew where the gels were kept in a drawer. He gave this information to Volker, who took one of the gels (shown in **Figure 3**) and set up a place on a lab bench to locate the bands, using a needle to poke through the autoradiogram and thereby mark the dried gel, with the aim of cutting out the small parts corresponding to the radioactive proteins. Although the amounts of 32P radioactivity were too small to be harmful, common safety practice was to set up a Plexiglass shield between the radioactive material and one’s body. Also common practice was to have a portable Geiger counter on hand; its “ticking” could be used to follow the radioactive material and to scan for contamination.

 After having set up this work station and placing the dried radioactive gels behind the shield, Volker quickly realized that the 32P radiation, as recorded on the Geiger counter, appeared to be passing unattenuated right through the shield, as if violating the laws of physics! This was a real “Eureka!” moment for him. Everyone who has worked with 32P and 35S knows that Plexiglass stops all of the beta rays emitted by these isotopes. Hence the conclusion was immediate that the supposed 32P-phosphate-labeled proteins didn’t have any 32P attached to them at all. Of the radioactive isotopes commonly used in biochemistry labs, Volker realized that only 125-iodine emits radiation (gamma rays) that pass through Plexiglass. Radioactive iodine can be chemically coupled to proteins very easily, and this was a well-known way to radioactively “tag” purified proteins of interest, a technique that was occasionally used both in the Racker and the Vogt labs. It came in a flash—the radioactive bands on all of those gels were not what they were claimed to be! The data had been fabricated in an obvious but cunning way. Volker was stunned. He immediately concluded that everything else Spector claimed to have done also must also be fraudulent. Careful examination of all of Spector’s published papers further convinced him that all of the supposed purifications of the ATPase and the four kinases also were fraudulent.

 On a Sunday evening two days after this finding, Volker met with Ef to apprise him of the finding of the 125-I labeled proteins, and to discuss how to proceed. Being convinced that everything Spector had done was fraudulent, and not being a member of Spector’s thesis committee or having any other official role, Volker decided to cease totally in having anything to do with Spector. Ef agreed that the iodinated proteins represented some sort of fraud, but he did not believe that all of Spector’s results were faked, and so he decided to give Spector two weeks to come up with the “real” ATPase and kinases. Not surprisingly, Spector was not able to produce any of the proteins, and he withdrew from the Graduate School.

 A half year later, after Spector’s connection with Cornell had been terminated and most of the press had lost interest in the case, Spector’s own notebook showed that immediately after he arrived at Cornell he began to assemble an arsenal of tools to perpetrate fraud. The very month he arrived, in January 1980, he recorded experiments to check how well a dozen inexpensive proteins that were available in any lab could be labeled with radioactive iodine. Indeed, a search in Spector’s notebooks uncovered the “Rosetta Stone”, a few pages that recorded his double bookkeeping underlying the kinase cascade. Although the identity of the proteins changed somewhat over time, at least in some experiments one subunit of the ATPase was carbonic anhydrase. PKM, PKS, PKL, and PKF were soybean trypsin inhibitor, glyceraldehyde 3-phosphate dehydrogenase, ovalbumin, and pyruvate kinase, respectively—all cheap proteins that one could purchase. Almost certainly his work on photosynthesis before coming to Cornell [1] also was faked—from its molecular weight the protein he claimed to have purified most likely was bovine serum albumin.

 The supposed ATPase perhaps deserves special comment. ATPase assays were routinely run in the Racker lab, and Spector certainly carried out plenty of such assays. But what he used as an ATPase apparently was a chicken virus called avian myeloblastosis virus (AMV), a close relative of the RSV retrovirus studied in the Vogt lab. AMV is shed into the serum of infected, leukemic chicks in vast amounts, over a hundred-fold higher than any other known retrovirus in any system, and so the virus is easy to purify and could be purchased. For reasons that are still not clear in the 21st century, when the AMV virus assembles at and buds from the infected chick myeloblast membrane, it incorporates into the viral membrane a host cell ecto-ATPase, i.e. an ATPase enzyme that is active on the surface of the virus. Both the Vogt and the Racker labs had abundant AMV on hand, and a previous post doc in the Racker lab had tried to purify this enzyme [7]. Ef used to marvel how surprisingly active this enzyme was, even though it represented only a tiny fraction of the viral protein. It was easy for Spector to use the virus as a surrogate for the Na-K pump he claimed to have purified. Ironically, months before the discovery of the 125-I labeled proteins, Ef had asked someone in the department to look by electron microscopy at what Mark claimed to be the partially purified Na-K ATPase. The pictures showed lots of virus particles (i.e. AMV), leading Ef to the erroneous conclusion that the mouse ascites cells, and therefore the mice from which they were derived, were infected with a virus. He then ordered the entire mouse colony to be destroyed.

 In cases of scientific fraud, the denouement in the form of a published retraction sometimes brings both clarity and closure to the case. Exactly the opposite applied to the retraction of Spector’s Cell paper in 1981 [8], co-authored by Pepinsky, Vogt, and Racker. That retraction was ambiguous, and to many researchers it seemed almost pathetic. It read, “*We have recently discovered a major discrepancy in an unpublished experiment involving the kinase cascade. This, together with several other findings, makes us doubt the correctness of the results reported in our paper published in Cell in July 1981. In particular, we believe that the immunological identification of PKF and the phosphoamino acid analyses may not be right. Thus, until we or others are able to reproduce the purification and the characterization of the kinase, the conclusions of the article must be regarded as unsubstantiated”*. The “unpublished experiment” was an oblique reference to the gels doctored with125-I labeled proteins. Despite Spector’s outrageously fraudulent data, the retraction made no mention of “fraud” and did not offer even a clue to the meaning of “major discrepancy”. This failure to be explicit may be explained in part by the short time between the finding of the fraudulent gels and composition of the retraction. Ef believed at the time that some of Spector’s results probably were correct, but he wasn’t sure which. Moreover, since Spector never admitted to any falsification whatsoever, Cornell administrators advised against writing anything that might have legal repercussions.

 The discovery of fraud in the Spector kinase cascade was, in emotional terms, very hard on Ef, since he had widely touted Mark as a prodigy, and had even sought to set Mark up as an independent researcher in part of the Racker lab. In the first year or two after the debacle, Ef had some of his lab members pursue aspects of Spector’s results, since he was convinced that some of those results were real. However, no solid confirmations came of these attempts. By 1989, when Ef wrote a commentary in *Nature* on scientific misconduct [9], mostly devoted to summarizing the Spector affair, he had dropped the idea that any of the Spector data were authentic. This article suggested that misconduct by “professionals” like Spector, who set out to mislead from the very beginning, is different and also more rare than misconduct that results from “fudging” to make real data look better or more convincing.

 What happened to Mark Spector after 1981? He eventually moved to Iowa and obtained a degree in osteopathic medicine. Almost exactly ten years after discovery of the fraudulent results at Cornell, on May 19, 1991 the Sunday Des Moines Register carried this headline: *“Web of deceit unfolds in wake of imposter’s great fall from grace”*. The story describes how Spector had been assisting a team of well-known physicians in cardiac surgery. The medical staff there predictably had found him to be brilliant. Mark had claimed to have both a DO and an MD degree. But through his involvement in a computer scam, it eventually was discovered that he had falsified the information about his MD degree, which then led to unearthing the scientific fraud at Cornell a decade earlier. Many people who first hear about the Spector affair think immediately of the 2002 Spielberg movie “*Catch Me If You Can*”.

Although the data supporting Spector’s kinase cascade were faked, some of the published results were correct in a technical sense. For example, in the Cell paper purporting to show the identity of PKL and Src, the peptide mapping was done correctly. But unbeknownst to Pepinsky, who carried out the mapping with a technique he had developed in the Vogt lab, the proteins used were not kinases, which never existed, but cheap purchased proteins provided Spector. Perhaps more important, the concepts underlying the cascade proved to be entirely valid. Precedents for protein kinases phosphorylating and thereby activating other enzymes were already known at that time (for example in glycogen metabolism), and in that sense Spector’s concepts were hardly novel. Then in the decades since 1981, many examples of kinase cascades were uncovered, especially in signal transduction, which describes the process by which extracellular signals (e.g. growth factors) are relayed to the nucleus to ultimately affect gene expression. A famous example is the phosphorylation and activation of one kinase by another in the “mitogen activated kinase” (MAP kinase) cascade. Ironically but perhaps not surprisingly, the term “kinase cascade” became tainted by the Spector fraud, and hence did not come to be widely used again until the 1990s.

 Many articles and chapters have been written about the Spector story, in the summer of 1981 in journals like *Discovery*, *Science*, and *Nature,* and later with more perspective in books like Broad and Wade’s “*Betrayers of the Truth: Fraud and Deceit in the Halls of Science*” (1982). Perhaps the most complete is in the form of an MS thesis in the science writing program at Johns Hopkins University, by former grad student Nicholas Zagorski (PhD Cornell, 2003). One of the many questions invariably raised by all popular articles was, “How could Spector’s falsification of data fail to have been detected over the one and a half years he was at Cornell, despite abundant warning signals?” Diverse answers are possible, and perhaps no single one is sufficient. Some would say that preventing scientific fraud requires more oversight of research workers, by mentors and coworkers and even perhaps by governmental agencies. The progress of experimental science is rooted deeply in reproducibility of results. If a measurement cannot be reproduced by multiple independent laboratories, it is regarded as unsubstantiated and then gradually is forgotten. To that extent experimental science is self-correcting, and arguably needs little regulation top-down. Furthermore, at some level all science is based on trust, though the trust that is modulated by criticism. The corrosive nature of mistrust arguably would do more harm than good to prevent cases like that of Spector. To quote a 17th century aphorism that Ef himself used, from the popular philosopher Rochefoucauld: *“It is more ignominious to mistrust than to be deceived”.*

**FOOTNOTES**

*Footnote 1*.
In early 1981 the nature of Ras, the protein product of the *ras* oncogene, was unknown. In his kinase cascade scheme, Spector assumed that Ras was a tyrosine kinase like Src and the several other protein kinases that had been linked to oncogenesis. But for once he was wrong: Ras was found later to be a GTPase, a “molecular switch” protein that turned out to be the founding member of a large family of some hundred structurally related eukaryotic proteins that control different cellular processes.

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**FIGURE LEGENDS**

**Figure 1. Outline of kinase cascade.** The diagram is copied from the cover of the abstract booklet provided to the participants of the 1981 Cold Spring Harbor conference on RNA Tumor Viruses. The four supposed kinases are in bold rectangles, with the small boxes in each denoting if the protein is phosphorylated on serine, threonine and/or tyrosine. Solid arrows indicate phosphorylation. The diamond-shaped boxes on the left are tyrosine-specific protein kinases known by 1981 to be involved in the tumorigenesis by these viruses (top to bottom): Rous sarcoma virus (v-Src protein), Y73 avian sarcoma virus, Abelson murine leukemia virus, feline sarcoma virus, PRCII avian sarcoma virus, Fujinami avian sarcoma virus, Harvey murine sarcoma virus (later identified as coding for the v-Ras protein).

**Figure 2. Example of 125-iodine labeled proteins on SDS-PAGE.**  The gel purportedly shows immune precipitates of crude extracts of NRK cells (a normal rat kidney cell line) and B-77 NRK cells (the same cells oncogenically transformed by the B77 strain of RSV). The cells, which were obtained from the Vogt lab, were purportedly labeled with 32P-phosphate. The rabbit anti-sera were supposedly against PKF, PKL, PKS, and PKM, as labeled over each lane. The autoradiogram appears to show that in the cancerous cells, but not in the normal control cells, the four kinases become phosphorylated. Note the identical pattern of background bands in all four lanes in the NRK series, which is an implausible result for four different antisera.

**Figure 3. Example of 125-iodine labeled proteins on SDS-PAGE.** The gel purportedly shows the results of radioactive labeling of Moloney murine leukemia virus-transformed hamster cells with 35S-methionine or with 32P-phosphate. Crude extracts from these cells were supposedly immune precipitated with the four individual antisera to the kinases. Since these are oncogenically transformed cells, both 35S and 32P labeled cells show kinase bands. The second lower molecular weight dark band in the PKF lanes presumably represents a mistake in setting up this faked experiment. Note the identical intensity of the 35S and 32P, which is wholly implausible. *(As shown by the barely visible pinpricks circling each dark band, this is the actual gel used by Vogt to uncover the 125-iodine doctoring.)*