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Eichmann K. The Network Collective. Rise and Fall of a Scientific Paradigm.

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Fields of medicine: Immunology, philosophy of science. The book tells the personal story of an immunologist who successfully worked on idiotypic network research, which gradually lost its presumed significance and vanished from the research literature.

Format: Hardcover

Audience: The book covers the rise and fall of the 4 concepts of the immune response regulation: idiotypic network, suppressor cells, Ir-genes, and nature of T-B lymphocyte cooperation. Although intellectually very attractive, the first concept was not confirmed to have the presumed physiological role and vanished from the literature and laboratories. The second proved nonexistent and the intellectual contribution invested in immense research literature turned out to be fruitless. The third also proved nonexistent but enhanced the understanding of the role of the major histocompatibility complex (MHC) genes and thus brought a Nobel Prize to one of its discoverers. The fourth was explained through deciphering the puzzle of the nature of T-cell receptor, and also led to a Nobel Prize. Nowadays, the first 3 concepts are history and are not interesting except for historical reasons. These reasons include not only the philosophical desire to understand the rise and fall of a scientific paradigm, but also the elucidation of what in the story was wrong, intellectually and materially. However, the chance to find scholars who may tackle the issue from the ethical point of view is dim. Among the handful of those who are left to read this book, there is only a few who had been involved in the story enough to understand it, and little enough not to have been affected with its unpleasant facets. I believe that this group does not consist of many more members than one – me.

Purpose: The question of purpose of this book, I believe, remains unanswered, and it should remain so. The author's intention was neither revisionist one nor a revival of the issue, the accusation (of others), mourning, or offering another view or interpretation. The delayed interviews with the actors do not provide the clue. I am afraid that the reader other than a historian of science or researcher of responsible conduct of research will understand less about the paths of scientific thought and work after reading the book than before it. This is despite the heroic and successful effort of the author to present his thoughts clearly, facts correctly, and actors fairly. In an unexpected, contradictory manner, these facts further obfuscate the purpose of the book.

Content: The book consists of 3 parts and an appendix that lists repeatedly mentioned and quoted researchers. The first part dwells on the philosophy of science, elegantly depicting the doubts on the nature of scientific knowledge. I love such texts, despite the fact that they regularly take me to my childhood Catholic Sunday-school lessons which told the same, but in a much more clear and sincere manner: only God knows what we are doing here. Consequently, I stick to scientific positivism, practiced by scientific and despised by intellectual Ego of every researcher.

The second part is the tough one: it embarks (though with the strong and noble hand) to the dark high seas of basic immunology, facing its most complicated parts such as the interactive theory of immunity, idiotypic network theory, T cell receptor puzzle, suppression that turned idiotypic (it did not!), and even the bedside virtues of idiotypy, which have always been hopeless, so much more today.

No need to read this part. Those who do not know it, will get lost, and those who know it, will get sad. The story is too complicated, too elusive, let alone that in a decade or two most of it cracked down as a huge, complicated research field that, to use Eichmann's term, yielded little "robust knowledge" (knowledge that the humankind can apply in the everyday life).

The third part of the book tries to unite discretely the first 2 parts – uncertainties of philosophy and of scientific practice. This prompts me to ask a simple question: "Do we have idiotypic network there or not? Even if it is ineffective, ie, lacking the key immunoregulatory role?" I would still admire it.

Highlights: Ir-gene concept had baffled me profoundly for several years, so much that I gave up on comprehending and using it in my modest scientific constructs. Fortunately, it relatively soon proved completely wrong, and this allowed full understanding of the function of MHC genes and antigens. It was more difficult with the idiotypic network theory, for it was so wise and elegant, so magically attractive; I was saved from plunging into the shallow sea by sheer luck – technical inability to start discovering anti-anti-antibodies (I was even unable to produce anti-anti-***b*** receptor antibodies by immunizing F1 hybrid by ***aa*** parental immune cells). But then, I paid a high price for being right on suppressor T-cells.

In the early 1980s, the population of T-cells was thought to contain some 50% of CD^{4+} helper cells and some 25-30% of CD^{8+} cytotoxic cells. Suppressor T-cells were allegedly hidden "among" those with the cytotoxic CD^{8+} phenotype. They were supposed to balance the function of the helpers, in a quite finely tuned manner. I could not understand how the Nature chose to "balance" 50% of a population (helpers) with a tiny, only functionally detectable, subpopulation of suppressors hidden among the 25% killers. Yet, the number of research reports and the authorities behind them discouraged me to spell out my doubts. I remember a meeting at which Dr Judith Kapp spoke on her suppressor cell model; I sat in the second row, determined to hear every word and see every number in her tables, and detect the cracks in the construction. In vain, the lecture was brilliant, self-assured, with impeachable data and great respect and admiration of the audience. I was not up to the task of open confrontation, and took a different approach.

In 1983, in Jan Klein's laboratory in Germany I offered a lecture on the subject. I worked there and knew the people, the meeting was informal, and I thought I could afford a small challenge. My friend Jan, who liked good humor, sat in the first row laughing in advance with Zoltan Nagy at my expense. Jan is a big man, so I started my lecture with the play of words: "When I was small, I wanted to grow up; when I grew up, I wanted to be Jan Klein. Because, if I were Jan Klein, I would know that there were no suppressor T-cells..."

They stopped laughing and looked truly angry. I continued, and they disliked the talk more than I expected. Jan interrupted me by asking angrily: "Matko, do you find it more important that a hypothesis is true or beautiful?!," and when I calmly and readily opted for beauty, they stood up appalled and left the room. Then everybody left the room. The only other Croat in the room was my younger friend Stipe Jonjić, visiting my lecture from the neighboring laboratory; he approached me, heavily shaken, green and pale in face, hugged me and offered to buy me a beer. It was his worry and pity that shocked me, and I gave up the idea of writing that suppressor T-cells did not exist. So, Moller did it in 1988.

Limitations: Dr Eichman failed, or better to say, avoided to offer more in-depth explanations on how and why so many people in so many experiments obtained data that ended up being either useless or wrong. However, it is hardly possible that so many fine minds just did not think hard enough, let alone all the hard work and money invested. One must ask how much of this is fraud or concrete fabrication and/or falsification, not to mention ethically questionable insistence on a concept that one's own data do not support. Research integrity apart, I believe that the issue offered an opportunity to philosophically encounter the question of the moral justification of the innumerable experiments published in the most prestigious journals, presented at numerous meetings, that were so profoundly far from the facts of Nature, yet simultaneously interpretationally consistent! Is it really true that somebody demonstrated the eighth-level of anti-anti-anti (8 times so)-antibody? What about Gershon et al's (eg, ABA) suppressor circuits, which indeed could have been wrongly envisioned, but the data on which these concepts were elaborated must have been there... or not? If the data had been sound and real, it would have been logical and evident to – reinterpret them. Was suppression there or not? If it had been, it could not have disappeared, regardless of whether the authors saw its mechanisms/circuits differently from how they truly worked.

Dr Eichmann may not be sorry for having been the part of the story, but I definitely am. Not only that, Dr Eichmant gave me a disappointment greater than those with idiotypy, immune suppression, and Ir-genes. This disappointment has to do with the puzzle of that time on the nature of T-B cell collaboration. This was my expertise, and there I had good data and firm opinions. Dr David Katz was my favorite authority in the field; he devised the scheme that T- and B-cells physiologically recognize each other by recognition of their identity at Class II region of MHC. My experiments were concordant with the picture, and I loved the simplicity and symmetry of the perfect physiological scheme (I called the cooperation "forming of the new organ at the place where it was needed," ie, at the place of encountering a foreign antigen). I remained Katz's follower even after he gave up his theory, which he did because the concept offered by Doherty and Zinkernagel became the "robust knowledge," and they were awarded a Nobel Prize for it. Now, in the interview part of the book, Dr W. Paul tells the story of Dr Katz's elegantly demonstrating soluble suppressor factors in a number of experiments, which the laboratory could not repeat a year later.

Like Dr Eichmann, in these cases, decent people in decent books (and journals) resort to the philosophy of science. So, at the end, I will quote Karl Popper: "Every refutation should be regarded as a great success; not merely a success of the scientist who refuted the theory, but also of the scientist who created the refuted theory and who thus in the first instance suggested, if only indirectly, the refuting experiment."