I come from a family of lawyers. When I was growing up, the only scientist in the family was my uncle, who was a physicist. But I was interested in science, and as a boy collected rocks and kept my “chemistry cabinet” in a spare room at my father’s law firm in Rome where I smelled up the place from time to time with failed experiments. When I finished high school at the Liceo Classico Torquato Tasso in Rome, I was, however, at a crossroads, trying to decide whether to pursue a career in science or medicine, both of which provided a way to positively influence the world. It seemed to me that medicine tackled problems “one patient at a time,” while science promised to be able to get to the root of a problem to solve it once and for all.

I did my studies at the University of Rome where, mentored by Professors Gino Doria and Luciano Adorini, I got my Doctor of Biological Sciences degree in 1984. Gino and Luciano had a strong influence on my choice of a career in immunology, and immunology seemed the perfect solution to that earlier dilemma of science versus medicine, as it was emerging as a discipline based on solid scientific rigor but at the same time had direct medical application. Plus, little did I realize at the time how relevant immunology would be to another emerging interest of mine, computers. In fact, one of my early papers, published in 1986 with Gino and Luciano, described computer code specifically designed for immunological applications.

By then, encouraged by my academic mentors, I knew that to gain exposure to the highest impact science I would have to do a post-doc in the US. I was thoroughly committed to immunology, so I was delighted when Gino and Luciano arranged for me to meet John Kappler and Pippa Marrack at National Jewish Hospital in Denver who, along with Howard Grey, led a top-notch immunology group, pushing forward the frontiers of T cell immunobiology. All 3 were already giants in the field of basic immunology, and all would later become members of the National Academy of Sciences. Howard interviewed me during my visit with John and Pippa and offered me a job on the spot. I was not sure why: although I was very determined and enthusiastic, the only thing I was interested in was making MHC-associated peptide binding site. In 1988, San Diego biotech pioneer Ted Green convinced Howard to leave Denver to head Cytel, a new biotech company in La Jolla whose mission was to develop immunomodulator drugs, based on blocking the MHC peptide binding site. In Denver, I was still hard at work characterizing peptide binding to MHC, and the idea of relocating to a place as beautiful as La Jolla was how a single MHC molecule could recognize so many different peptide antigens (epitopes) and still retain specific binding. We were able, with the aid of an Apple IIe computer housed in a corner of my bedroom, to detect that different MHCs indeed had direct medical application. Plus, little did I realize at the time how relevant immunology would be to another emerging interest of mine, computers. In fact, one of my early papers, published in 1986 with Gino and Luciano, described computer code specifically designed for immunological applications.

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primary interest had again become focused on development of lead candidates for anti-HIV and anti-cancer vaccines, and early technological development became less of a focus. I recall thinking, right after 9/11, that the time was right for me to get back into more basic science. Meanwhile, Howard Grey had become president of La Jolla Institute for Allergy and Immunology (LJI) in 1995, and in 2003, right before he stepped down and passed that torch to Mitch Kronenberg, Howard and Mitch recruited me to LJI to start an Initiative for Emerging Diseases and Biodefense from scratch. I have been a faculty member at LJI ever since.

One project that has continually occupied me here, perhaps as a testament to my early interest in computer and immunology, is to develop and manage the immune epitope database (IEDB: http://www.iedb.org), a freely available resource funded by the National Institute of Allergy and Infectious Diseases (NIAID). The IEDB catalogs all epitopes for humans, non-human primates, rodents, and other vertebrates, from allergens, infectious diseases, autoantigens and transplantation epitopes and today includes almost one million epitopes derived from almost 20,000 different literature reports. Investigators can also use the website to access the Analysis Resource, a collection of bioinformatics tools useful to analyze epitope data or predict epitopes.

In terms of research, I am now a Professor and Head of the Division of Vaccine Discovery at LJI, and my lab focuses on understanding immune responses to many different targets, from infectious diseases like TB, whooping cough, dengue or Zika, to allergies and asthma caused by pollens, cockroaches and dust mites, to autoimmunity and neurodegenerative diseases and cancer. Overall, however, whether we study an infection like TB or severe reactions to seasonal allergens, our work is based on the same fundamental idea: namely, to compare immune responses at the molecular level in “good” vs. “bad” outcomes to reveal key hidden differences that could be applied to design of immune treatments that mimic the good ones.

For example, we study disease susceptibility among individuals from regions highly infested with mosquitoes carrying dengue virus: some people acquire resistance to dengue disease, while others contract a severe hemorrhagic form of the disease. At the same time our group has been involved in evaluating a promising dengue vaccine candidate and shown that immune responses to that vaccine resemble those exhibited by individuals who develop natural immunity. Our studies relevant to allergy are another example. In this case, we are studying differences in immune responses. We all are exposed to pollen and common allergens during allergy season, but only some individuals develop severe allergy while most of us don’t. It turns out that the immune system of non-allergics also “sees” pollen but instead of generating a harmful response gives rise to a “healthy” one. As a result, our goal is to improve conventional “allergy shots” administered to patients by making sure they induce an immune response that resembles that seen in allergy-free individuals.

So while my current work may appear to cover a lot of bases, conceptually it has a continuity that goes back 30 y. I was one of the early participants in a “peptide revolution” of sorts, which in the early 80s allowed us to study and produce relatively cheaply synthetic peptides and unequivocally define what immune cells T cells really see, and how immune responses are
stimulated. I published my first study of a peptide epitope back in 1984, and more than 30 y later, I still love what I do, either as a peptide revolutionary or an epitope geek. The bioinformatics tools and databases we use in research every day, although no match for the microcomputer I wrote my first computer program on, helped drive that revolution, like computational tools are driving most of biology.

And finally, allow me one more story about the person who set me on this path. When he stepped down as LJI president in 2003, Howard Grey stayed on in La Jolla and worked in my lab there for another 10 y as a partner and key contributor in driving grant funding. When he retired 2 y ago, we had been colleagues from 1985 to 2014. As my most influential scientific mentor, Howard was blunt and I liked that: he had a razor-sharp capacity to get to the bottom of things. Plus, he had a complete lack of ego and expected you to drop a hypothesis if it was not supported by experiments, something he was equally ready to do. But he was also a personal mentor. Both my parents had died before I moved to the US so Howard became a father figure. He was the “main man” at my wedding! Just one of the smartest people I ever met.

Of course, my work would not have been possible without many other collaborators as well, both at LJI and around the world. It is particularly satisfying at this point in my career to know that people in our field, and in vaccine development in particular, now have tools to address some really challenging questions—What kind of T cell response would be protective against a disease? Why do some immune responses control infection while others don’t? Could a particular peptide antigen be developed as a more effective immunotherapy for allergy or asthma? I believe we can answer these questions. I remain an unrepentant optimist.