In memoriam to Vittorio Ricci, Professor of Pathology, Pavia University

My great friend Vittorio Ricci died suddenly May 4th 2020.

I met Vittorio for the first time in Washington in 1997 where the big meeting on Gastroenterology was taking place. It was at one of the poster sessions, where Vittorio was presenting data on the vacuolating toxin of *Helicobacter pylori* (VacA), that we actively discussed for the first time. The study of this toxin was one of my laboratory new topic in Nice. One of my student Antoine Galmiche had started his PhD on the mode of action of VacA which was unkown at that time (excepeted the vacuolating activity) and as a « mise en jambes » was trying to reproduce data on VacA from a proeminent italian group working on VacA. However, Antoine could not at all reproduce these data and complained to me that the topic was quite cumbersome. I discussed with Vittorio about this problem and we imagined some putative mode of action of this fascinating toxin for a cell biologist.

At the beginning of 1999 I got a letter from Vittorio asking me for a post doctoral year in my laboratory in Nice to study VacA. Vittorio got easily a financial support from INSERM. In the fall of 1999 Vittorio was in Nice and, using the cell biology tools that we had, started to study the mechanism by which vacA is taken up by cells. Rapidly, he found that VacA was endocytosed by a clathrin-independent pathway and that lipid rafts were absolutly required for the toxin cell binding (1) Later on, he helped Antoine for his thesis who finally found that mitochondria were targets for VacA and inducing cell death (2). All these data were fully confirmed by different groups among the world.

Vittorio returned back in Italy in 2000 but our fructfull collaboration was still on between Pavia and Nice. In Nice a new student, Nils Gauthier , started his PhD on the study of the intracellular traficking of VacA. With the great help of Vittorio, who furnished fully active fluorescent labeled VacA, Nils beautifully with rhis tool demonstrated that VacA was endocytosed by a newly described clathrin-independent pathway named the CLIC/GEEC mechanism (3). In fact this is actually a key point to understand why T and B lymphocytes are sensitive and killed by VacA.

Again, some years later in closed collaboration with Vittorio we showed that the CagA molecule (cytotoxin associated to VacA) injected by a type VI mechanism by the *Helicobacter pylor*i into gastric cells (when the bacterium colonizes the gastric epithelium) (4) in fact counteracted the deleterious effect of VacA on the gastric epithelium deciphering thus a new virulence bacterial strategy (5, 6).

Just before the disparition of Vittorio and in collaboration with my ex student Nils Gauthiers, who works actually at the IFOM in Milano, we were actively working on new mechanisms of CagA and VacA. In memory to Vittorio we hope to finish up these works which will be dedicated to Vittorio.

Good bye Vittorio you was like king Midas; everything you touched became gold.

1/ Mol. Cell Biol. (2000) 11 : 3897-3909
2/ EMBO J. (2000) **19** vol 23 : 6361-6370
3/ J. Cell Biol. (2007) **177** : 2 343-354
4/ Curr.Opin.Microbiol. (2008) **11** : 30-37
5/ PLOS Pathogens (2009) **5**, 10 : e 1000603
6/ PLOS Pathogens (2009) 6, 9 : e 1001057

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