

# CURRICULUM VITAE

## RINO RAPPUOLI

### Business address

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### **Current positions**

2015 - to date Chief Scientist and Head External R&D, GlaxoSmithKline Vaccines (Siena, Italy).  
2020- to date Honorary Professor of Vaccinology, Faculty of Medicine, Department of Infectious Diseases, Imperial College (London, United Kingdom) and Professor of Molecular Biology, University of Siena (Siena, Italy)

### Previous positions

**2017 - 2019** Professor of Vaccines Research, Faculty of Medicine, Imperial College (London, United Kingdom)

**2014** Global Head Research and Development, Novartis Vaccines (Siena, Italy).

**2007-2015** Founder and chairman of the Board of the Novartis Vaccines Institute for Global Health (Siena, Italy).

**2006** Global Head Vaccines Research, Novartis Vaccines & Diagnostics (Siena, Italy).

**2003** Chief Scientific Officer and Vice President Vaccines Research, Chiron Corporation (Emeryville, USA).

**1996** Vice President Vaccines Research, Chiron Corporation (Emeryville, USA).

**1992** Head of Research of IRIS, the Chiron S.p.A. Research Institute (Siena, Italy).

**1988-1991** Head of the Sclavo Research and Development (Siena, Italy).

**1985-1987** Head of the laboratory of Bacterial Vaccines at the Sclavo Research Center. Worked on the molecular genetics of *Bordetella pertussis* and the development of a new vaccine against whooping cough.

**1982-1984** Sclavo Research Center, Worked on the molecular biology of *Corynebacterium diphtheriae* and the development of a new vaccine against diphtheria.

**1980-1981** Visiting scientist at the Harvard Medical School (Boston, USA). Worked on the molecular biology of bacteriophages of *Corynebacterium diphtheriae* in the laboratory of John Murphy.

- 1979** Visiting scientist for four months at the Rockefeller University (New York, USA). Worked on the purification of gonococcal antigens in the laboratory of Emil Gotschlich.
- 1978-1984** Staff scientist at the Sclavo Research Center (Siena, Italy).

### Education

- 1972-76** Undergraduate in Biological Sciences at the University of Siena.
- 1975** Four months at the Center for Biological and Natural Systems (Washington University, St. Louis, USA), working on bacterial mutagenesis from carcinogens.
- 1976** Obtained the doctoral degree in Biological Sciences at the University of Siena (with honours). The experimental thesis concerned the use of NMR in biological systems.
- 1977** Military service

### Honors

- 1989** Scipley Lecturer (Harvard Medical School)
- 1990** Elected member of the European Molecular Biology Organization
- 1991** Paul Ehrlich and Ludwig Darmstaedter Prize (Germany)
- 1991** "Federchimica" award (Italy)
- 1992** European Federation Pharmaceutical Industries Association Award (EFPIA), for the best biotechnological product.
- 1992** "Scanno" award (Italy)
- 1992** Eighteenth Maxwell Finland Lecture (Harvard Medical School)
- 1993** "Galeno" award (Italy)
- 1994** "Philip Morris" award (Italy)
- 1994** "Lepetit" award (Italy)
- 1996** "Federchimica" award (Italy)
- 1998** Dr. Friedrich Sasse Award (Germany)
- 2002** Arima Award for Applied Microbiology (IUMS)
- 2002** Distinguished Visitor Award (University of Auckland)
- 2003** City of Florence Award for Molecular Sciences (Italy)
- 2004** Galeno award (Italy)
- 2005** Gold Medal awarded by the Italian President for contributions to public healthcare
- 2005** Election to U.S. National Academy of Sciences
- 2007** Miami Nature Biotechnology Winter Symposium Special Achievement Award
- 2009** Albert B. Sabin Gold Medal Award
- 2009** Antonio Feltrinelli Award
- 2010** Life Achievement Award for Scientific Excellence, Institute of Human Virology, University of Maryland
- 2011** Excellence Award from the European Society of Clinical Microbiology and Infectious Diseases
- 2012** Assobiotec Award
- 2013** Nominated third most influential person worldwide in the field of vaccines (Terrapin)
- 2014** Nominated fourth most influential person worldwide in the field of vaccines (VaccineNation)
- 2014** Prix Galeno Italy, UK, and France for the best pharmaceutical product
- 2015** Fellowship Faculty of Medicine (Imperial College London)
- 2015** Hilleman Award (American Society for Microbiology)

<b>2016</b>	Election Foreign Member (Royal Society, London)
<b>2017</b>	Canada Gairdner International Award
<b>2017</b>	Lifetime Achievement European Inventor Award
<b>2017</b>	Election Foreign Member (American Academy of Arts & Sciences)
<b>2018</b>	President Elect International Union of Microbiological Societies (2020-2023)
<b>2019</b>	Robert Koch Award
<b>2020</b>	Honorary doctorate degree University of Wurzburg, Germany

### **International Associations & Committees**

- European Molecular Biology Organization (EMBO)
- American National Academy Science (NAS)
- American Society for Microbiology (ASM)
- International Society of Toxinology
- Founder member of the International Society for Vaccines (ISV)
- Chairman of the Expert Panel COST/STD Initiative on combined vaccines (1995-1996)
- Chairman of the R/D Working Group of the European Vaccines Manufacturers (EVM)
- Member of the Scientific Council of the Paul Ehrlich Foundation (1996-2014)
- Member of the Scientific Council of the International Institute of Genetics and Biophysics (Naples, Italy; 1997-1999)
- Member of the Research Directors Group (RDG) within the European Commission
- Served in many committees, among which the NIH Search Committee for the Director of the Vaccine Research Center (Bethesda, 1997-1998), and the Infection and Vaccinology International Board, a research programme funded by the Foundation for Strategic Research (Stockholm, 2000)
- Member of the WHO/PRD R&D Committee (1999-2000)
- Co-chairman of the R&D Task Force of the Global Alliance for Vaccines and Immunization (GAVI, 2000-2001)
- Institute of Medicine. Committee on Identifying and Prioritizing New Preventive Vaccines for Development – SMART Vaccines (2009-2015)
- Core member (2009) and Board member (2015) of the European Academy of Microbiology (EAM)
- Elected member of the European Academy of Tumor Immunology (2011)
- Panel member of the Institut of Medicine for new vaccines (2011-13)
- Member of R&D group of the Decade of Vaccines (2011-12)
- Chair of the European Research Council (ERC AdG) – LS7 panel (2008-2012)

### **Scientific Journals**

Member of the Editorial Board of: *Science Translational Medicine*, *Archives in Microbiology* (1994-2002); *Biotec*; *Cellular Microbiology* (1999-); *Current Drug Targets – Immune, Endocrine & Metabolic Disorders* (2000-); *Current Opinion in Biotechnology* (2008-); *Current Opinion in Microbiology* (1998-); *Journal of Cell Biology* (1996-2003); *Investigational Drugs* (2001-); *Infection and Immunity* (1995-); *International Journal of Medical Microbiology* (2000-2007); *Molecular Microbiology* (1987-); *The EMBO Journal* (1993-1995); *Vaccine* (2000-); *mBio* (2009-); *Current Topics in Microbiology and Immunology* (2012-); *Journal of Experimental Medicine* (2017-)

Served as reviewer for: *Archives in Microbiology*; *Cell*; *Cellular Microbiology*; *EMBO Journal*; *European Journal of Cell Biology*; *Gastroenterology*; *Gene*; *Gut*; *Infection and Immunity*; *Microbial Pathogenesis*; *Molecular Microbiology*; *Nature*; *Nature Medicine*; *Proc. Natl. Acad. Sci. U.S.A*; *Science*; *Journal of Medical Microbiology*; *The Journal of Infectious Diseases*; *Vaccine*

## **Research grants obtained**

Many grants from NIH, HHS and DARPA for the activities carried out in the USA, including funding for discovery of new adjuvants (48 million), HIV (more than 100 million in 15 years), Pandemic influenza (several hundred million in R&D), and RNA vaccines (28 million). ERC Advanced Grant on human monoclonal antibodies for antimicrobial resistance and Covid-19.

## **Coordinator of the following European grants**

Mucosal Vaccines for Poverty Related Diseases European Initiative for basic research in Microbiology and Infectious Diseases - IAPP	European Commission	€15.500.00
Advanced Immunization Technologies – ADITEC	European Commission	€2.172.00
	European Commission	€30.000.00

## **Meetings and symposia**

**Keynote speaker** at many meetings including ASM (2008), ICAAC (2011), International Congress of Immunology (2013).

**Organizer** of Keystone Symposia meetings (Seattle 2010; Rio de Janeiro, 2013; Translational Vaccinology, 2017); Transforming Vaccinology (originally Florence 2020, due to Covid-19 it was changed to virtual meeting in June 2020) and, as of 2004, the annual international scientific exchange meeting organized on rotation in Italy, USA, Belgium (aka Palio Meeting).

**Publications** 715 publication in PubMed (H-index 137, total citations 74884).

**Books edited** More than 20 edited books that include: *Guidebook to Protein Toxins and Their Use in Cell Biology* (OUP, 1997); *New Generation Vaccines* (2004, 2009); *Cellular Microbiology* (ASM 2000, 2004); *Influenza Vaccines for the Future* (Springer, 2008); series editor of *Current Topics in Microbiology and Immunology* (Springer); Vaccines PNAS 100th Anniversary Special Feature (ASM, 2014); *Antibodies for Infectious Diseases* (ASM, 2015).

## **Scientific contributions and achievements**

**Precision medicine:** In 1989 he published a paper in *Science* describing the engineering of the bacterium *Bordetella pertussis* by making two precise codon changes in the chromosome. The engineered bacterium produced a fully immunogenic, but completely non-toxic form of pertussis toxin that was the basis for the development of an acellular pertussis vaccine that showed 84% efficacy against disease in clinical trial involving 16,000 infants.

**Genomics.** In 2000 he published a paper describing the discovery of antigens against meningococcus *B* starting directly from the genome of the bacterium. He called the new technology “Reverse Vaccinology” to underline the novel approach which allowed to discover new antigens directly from the genome information without the need to growing the pathogens. The vaccine derived from this discovery is now licensed worldwide and has shown effectiveness against disease of 83%.

**Synthetic biology.** In 2013 Rappuoli reported the first pandemic vaccine derived from synthetic biology. An RNA vaccine was generated in only one week starting from the nucleotide sequence downloaded from the internet.

In addition, Rino Rappuoli has made numerous outstanding contributions to medical science in the fields of vaccinology, bacterial virulence and immunology. He was an early advocate of structure-based rational vaccine design and is famous for ‘Reverse Vaccinology’, which exploits genomics to identify and characterise vaccine candidates, and which he used successfully to develop a licensed vaccine against meningococcus serogroup B. As an industry leader, he is unique in retaining very close ties with academia; he has protected and advanced fundamental research in the vaccine industry throughout his career. The main achievements are described below:

*Diphtheria and CRM197.* During the period 1980-84 Rappuoli developed *Corynebacterium diphtheriae* strains hyperproducing CRM197 (1), sequenced the gene for diphtheria toxin, and its non-toxic mutant CRM197. Since then CRM197 has become the carrier protein for conjugate vaccines used worldwide against *Haemophilus influenzae*, meningococcus and pneumococcus. Most of newborns worldwide today receive vaccines containing CRM197.

*Pertussis.* During the period 1984-95 Rappuoli cloned and sequenced genes coding for pertussis toxin (2). He used the sequence information to design and introduce two precise base pair changes in the chromosome of *Bordetella pertussis*. The engineered strain produced a fully immunogenic but non toxic form of pertussis toxin which was the basis for an acellular pertussis vaccine that showed 84% protection in phase III efficacy trial and was licensed in Europe (3). The acellular vaccine pertussis vaccine containing the nontoxic form of pertussis toxin represents the first precision medicine medical intervention approved for human use.

*Conjugate vaccine against meningococcus C.* In 1989 Rappuoli made the first conjugate vaccines against meningococcus A and C. In 1992 the development and clinical tests of the first conjugate meningococcal vaccines was published in *Vaccine* (4). This led to the establishment of a public-private partnership with the UK Department of Health that led to the vaccination of the entire UK population from 2 month to 18 years of age in 1999-2000 and the elimination of meningococcus C from the UK.

*Licensing of the adjuvant MF59 for human use.* In 1997, an influenza vaccine adjuvanted by the oil-in water emulsion MF59 by Rappuoli’s team was licensed in Italy. The same vaccine was licensed in Europe in 2000 and in USA in 2015. MF59 represents the first vaccine adjuvant licensed for human use after the introduction of alum in the 1920s. In 2011 a paper published in *The New England Journal of Medicine* (NEJM, 378:1406-1416, 2011) reported that the addition of MF59 to the influenza vaccine increases the vaccine efficacy in infants from 43 to 86%. Today, MF59 is a leading candidate for many vaccines, including pandemic influenza and Covid-19.

*Meningococcus B.* In 1996 Rappuoli began a collaboration with Venter and Moxon to sequence the genome of serogroup B meningococcus, with the idea of using the genomic information to develop a vaccine that up to that point had been impossible with conventional technologies (5). Rappuoli named the new approach **Reverse Vaccinology** (6); its application led to the licensure of the first Meningococcus B vaccine in Europe in 2013 and USA in 2015 (8). The UK Joint Committee for Vaccines and Immunization recommended the vaccine for infant immunization in 2014. In 2015 the UK Secretary of State for Health announced the decision to introduce the vaccine in the National Immunization programme. Since then the vaccine reduced the number of cases in the vaccinated children by 74%.

*Reverse vaccinology and the pangenome concept.* The genome-based discovery of novel antigens, pioneered by the meningococcus B vaccine, was applied by Rappuoli’s teams to many other bacteria including group B streptococcus and *Staphylococcus aureus*. While comparing multiple genomes for group B streptococcus, Rappuoli developed the concept of “pangenome” to include all genes present within a species (7).

*Pandemic influenza and synthetic biology.* Shortly after the first outbreak in humans of H5N1 in Hong Kong in 1997, Rappuoli did a phase I trial showing that the MF59 adjuvant was necessary to induce immunity against the avian influenza H5N1. The results were confirmed in many trials in

2004-2007 and led to the safe use of the adjuvant during the 2009 H1N1 influenza pandemic (9). In 2014 Rappuoli reported the first pandemic vaccine derived from synthetic biology. An RNA vaccine was generated in only one week starting from the nucleotide sequence downloaded from the internet (Hekele et al *Emerg Microb Infect* 2(8):e52, 2013). The same synthetic gene was used to generate a viral seed to produce in a record time a vaccine that was tested in a clinical trial against the emerging H7N9 strain (11).

*Structural vaccinology.* A decade ago Rappuoli recognized that the increasing throughput of protein structure determination by X-ray crystallography, Nuclear Magnetic Resonance, and cryo-electron microscopy would open the way for structure-based design of vaccine antigens. The name “structural vaccinology” was coined for the emerging field. Today structural vaccinology is a reality that provides greatly improved antigens for meningococcus (10), respiratory syncytial virus, and HIV.

*Human monoclonal antibodies.* In 2019 Rappuoli started a laboratory to develop human monoclonal antibodies for prevention and therapy of bacteria resistant to antibiotics. When Covid-19 pandemic started, his laboratory turned into the isolation of human monoclonal antibodies to the SARS-Cov-2 virus and reported the isolation of several neutralizing human monoclonal antibodies that can be used for therapy and prevention of Covid-19 (12).

*A non-profit institute to develop vaccines against neglected diseases.* Rappuoli founded the Novartis Vaccines Institute for Global Health (NVGH), officially opened in February 2008 and headed by Allan Saul. The institute had access to all technologies and know-how available at Novartis Vaccines and focuses on developing vaccines against neglected diseases. The Institute has been inherited by Glaxo SmithKline and has changed the name to GSK Vaccine Institute for Global Health (GVGH). In January 2020 the first vaccine developed by GVGH (typhoid conjugate vaccine) has been licensed in India.

*Policy.* Throughout his career, Rappuoli has championed the value that vaccines have provided and will provide to society. Key contributions have been the intangible value of vaccination, developing vaccines for an ageing society, editing a monographic issue of PNAS (2014) on the value of vaccination, and a supplement to PNAS in 2018 advocating vaccines to fight antimicrobial resistance.

## Top 20 publications

- 1 **Rappuoli, R.** (1983) Isolation and characterization of *Corynebacterium diphtheriae* nontandem double lysogens hyperproducing CRM197. *Appl Environ Microbiol* **46**, 560-564
- 2 Ratti, G., **Rappuoli, R.**, and Giannini, G. (1983) The complete nucleotide sequence of the gene coding for diphtheria toxin in the coryneophage omega (tox+) genome. *Nucl Acids Res* **11**, 6589-6595
- 3 Nicosia, A. et al ..... **Rappuoli, R.** (1986) Cloning and sequencing of the pertussis toxin genes: operon structure and gene duplication. *Proc Natl Acad Sci USA* **83**, 4631-4635
- 4 **Rappuoli, R.**, Perugini, M., and Falsen, E. (1988) Molecular epidemiology of the 1984-1986 outbreak of diphtheria in Sweden. *N Engl J Med* **318**, 12-14
- 5 Pizza, M. et al ..... **Rappuoli, R.** (1989) Mutants of pertussis toxin suitable for vaccine development. *Science* **246**: 497-500
- 6 Costantino, P. et al .... **Rappuoli, R.** (1992) Development and phase 1 clinical testing of a conjugate vaccine against meningococcus A and C. *Vaccine* **10**, 691-698
- 7 Cossart, P., Boquet, P., Normark, S., and **Rappuoli, R.** (1996) Cellular microbiology emerging. *Science* **271**, 315-316
- 8 Tettelin, H. et al .....**Rappuoli, R.**, and Venter, J. C. (2000) Complete genome sequence of *Neisseria meningitidis* serogroup B strain MC58. *Science* **287**, 1809-1815

- 9 Pizza, M. et al ..... **Rappuoli, R.** (2000) Identification of vaccine candidates against serogroup B meningococcus by whole-genome sequencing. *Science* **287**, 1816-1820
- 10 **Rappuoli, R.** (2000) Reverse vaccinology. *Curr Opin Microbiol* **3**, 445-450
- 11 **Rappuoli, R.**, Miller, H. I., and Falkow, S. (2002) Medicine. The intangible value of vaccination. *Science* **297**, 937-939
- 12 Lauer, P. et al ..... **Rappuoli, R.**, Grandi, G., and Telford, J. L. (2005) Genome analysis reveals pili in Group B Streptococcus. *Science* **309**, 105
- 13 Tettelin, H. et al .... **Rappuoli, R (corr author)** and Fraser, C. M. (2005) Genome analysis of multiple pathogenic isolates of Streptococcus agalactiae: implications for the microbial "pan-genome". *Proc Natl Acad Sci USA* **102**, 13950-13955
- 14 **Rappuoli, R.**, Del Giudice, G., Nabel, G. J., Osterhaus, A. D., Robinson, R., Salisbury, D., Stohr, K., and Treanor, J. J. (2009) Public health. Rethinking influenza. *Science* **326**, 50
- 15 Swanson, K. A. et al ..... **Rappuoli, R. (corr. author)**, Mandl, C. W., Dormitzer, P. R., and Carfi, A. (2011) Structural basis for immunization with postfusion respiratory syncytial virus fusion F glycoprotein (RSV F) to elicit high neutralizing antibody titers. *Proc Natl Acad Sci USA* **108**, 9619-9624
- 16 Scarselli, M. et al ..... **Rappuoli, R.** (2011) Rational design of a meningococcal antigen inducing broad protective immunity. *Sci Trans Med* **3**, 91ra62
- 17 Hekele, A. et al. Rapidly produced SAM((R)) vaccine against H7N9 influenza is immunogenic in mice. *Emerg Microbes Infect* **2**, e52 (2013).
- 18 Dormitzer, P. R. et al. Synthetic generation of influenza vaccine viruses for rapid response to pandemics. *Sci Transl Med* **5**, 185ra168 (2013).
- 19 Bloom, D.E., Black, S., Salisbury, D., **Rappuoli, R.** (2018). Antimicrobial resistance and the role of vaccines. *Proc Natl Acad Sci USA* **115**:12868-12871.
- 20 Andreano, E. et al ..... **Rappuoli, R** (2020), Identification of neutralizing human monoclonal antibodies from Italian Covid-19 convalescent patients. *bioRxiv* preprint posted 9 May 2020.