

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).

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)

2016 Election Foreign Member (Royal Society, London)

2017 Canada Gairdner International Award

2017 Lifetime Achievement European Inventor Award

2017	Election Foreign Member (American Academy of Arts & Sciences)
2018	President Elect International Union of Microbiological Societies (2020-2023)
2019	Robert Koch Award
2020	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* (2017-2019)

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).

Coordinator of the following European grants

Mucosal Vaccines for Poverty Related Diseases	European Commission	€15.500.00
European Initiative for basic research in Microbiology and Infectious Diseases - IAPP	European Commission	€2.172.00
Advanced Immunization Technologies – ADITEC	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 (Florence 2020) and, as of 2004, the annual international scientific exchange meeting organized on rotation in Italy, USA, Belgium (aka Palio Meeting).

Publications 707 publication in PubMed (H-index 134, total citations 71142).

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

Diphtheria and CRM197. During the period 1980-83 studied the genetics of bacteriophages of *Corynebacterium diphtheriae*. This resulted in the characterization of the phages carrying the gene coding for diphtheria toxin, the nucleotide sequence of the toxin gene and several genes coding for non-toxic mutants. CRM197, one of the mutants that was characterized and hyperexpressed, became a carrier for many conjugate vaccines against *Haemophilus influenzae*, meningococcus and pneumococcus. Today CRM197 is one of the most used molecules for immunization, and is given to most children worldwide

Pertussis. During the period 1984-95 approached the development of an acellular vaccine against pertussis. This work was characterized by the cloning and sequencing of the genes coding for the five subunits of pertussis toxin (1986), its side directed mutagenesis (1998), and the construction of a *Bordetella pertussis* strain producing a non-toxic form of pertussis toxin (1989). The vaccine containing this molecule was tested in phase I (1989-90), phase II (1991-2) and phase III (1993-95) efficacy trials. The vaccine showed high efficacy against clinical disease, it was licensed in Italy and Europe and used in humans since 1993. The mutant form of pertussis toxin used in the vaccine represents the first protein constructed by rational drug design that has been approved for human use.

Meningococcal conjugate vaccines. In 1989, following the promising results of conjugate vaccines against *Haemophilus influenzae*, made conjugate vaccines against meningococcus A and C. In 1992 the development and clinical tests of the first conjugate meningococcal vaccines was published in *Vaccine* (Costantino et al. *Vaccine* 1992; **10**: 691-698). In 1991-1993 phase I-II clinical trials started in The Gambia, United Kingdom, and the United States. The promising results in phase II studies encouraged the Public Health Laboratory Service (PHLS) in the United Kingdom to start a program for the clinical development of a conjugate vaccine against meningococcus C.

In 1999-2000 the vaccine was licensed in the UK, and by 2001 had eliminated most of the meningococcal C cases in the UK. Tetravalent conjugate vaccines to cover four strains (MenACYW) were developed and licensed worldwide.

Mucosal adjuvants. During the period 1992-99 used the technologies developed for pertussis to construct non-toxic derivatives of cholera and *Escherichia coli* enterotoxins. The systematic study of many non-toxic derivatives of these toxins resulted in the selection of two non-toxic mutants (LTK63 and LTR72) which are today believed to be the most promising mucosal adjuvants available.

Helicobacter pylori. During the period 1992-99 worked on this emerging pathogen. The main achievements were: the development of the first mouse model and the classification of the clinical isolates into pathogenic and less pathogenic strains (type I and II, respectively). The cloning, characterization and sequencing of several important antigens such as the Vacuolating cytotoxin (VacA), the cytotoxin-associated immunodominant antigen (CagA). The discovery of the presence of a pathogenicity island which is responsible for most of the pathogenesis of *Helicobacter pylori* and that this codes for a Type IV secretion apparatus, which injects the protein CagA into the host cells, which in turn phosphorylates the bacterial protein. A vaccine based on the major antigens entered the clinical development, however after a successful phase I it was put on hold, mainly for commercial reasons.

Cellular microbiology. In 1996 the review “Cellular Microbiology Emerging” (*Science*; 271: 315-316) by Cossart P, Boquet P, Normark S, **Rappuoli R** coined the term “Cellular Microbiology” to formalize the marriage between cell biologists and microbiologists. The new discipline was adopted by the scientific community and has since given vent to a series of meetings with this title, to the founding of a scientific journal, and to the publication of two textbooks.

Licensing of the adjuvant MF59 for human use. In 1997 his team licensed in Italy an influenza vaccine adjuvanted by the oil-in water emulsion MF59. The same vaccine was licensed in Europe and in many other countries in the year 2000. MF59 represents the first vaccine adjuvant licensed for human use after the introduction of alum in the 1920s. The MF59-adjuvanted influenza vaccine was widely used during the 2009 influenza pandemic. In 2011 a paper published in the New England Journal of Medicine reported that the addition of MF59 to the influenza vaccine increases the vaccine efficacy in infants from 43 to 86%. This led to the licensure of the vaccine in children in Canada in 2015. Today, MF59 is a leading candidate for many vaccines, including pandemic influenza. In 2016 the MF59 adjuvanted influenza vaccine was licensed by the FDA for vaccination of the elderly in the USA.

Reverse vaccinology and meningococcus B. During the period 1996-99 I started collaborating with Craig Venter at TIGR and Richard Moxon in Oxford to sequence the genome of serogroup B meningococcus with the idea of using this new technology to find novel antigens and develop a vaccine which had not been solved for decades using conventional technologies. The results were impressive and in a short period of time we found many novel protective antigens. The genomic approach to vaccine development was named *reverse vaccinology*. The vaccine deriving from the genome approach entered phase I testing in 2002. In November 2012 the European Medicinal Agency recommended the granting of a marketing authorization for Bexsero, the first vaccine to provide broad coverage against meningococcal serogroup B. This was followed by the approval of the European Commission in January 2013. In August 2013 the vaccine was approved by the Australian Register of Therapeutic Goods (ARTG) for use in individuals from two months of age and older. In February 2014 the Joint Committee on Vaccination and Immunisation (JCVI) recommended the inclusion of Bexsero in the UK National Immunisation Programme (NIP) for routine use in infants from two months of age. In January 2015 the US Food and Drug Administration (FDA) granted approval of Bexsero in adolescents and young adults from 10 years through 25 years of age. The data from the national immunization program in the UK confirm the very high efficacy of the vaccine in preventing meningococcus B disease.

Pandemic influenza. My team started working on avian influenza shortly after the first outbreak in humans of H5N1 in Hong Kong. A clinical trial in 2001 showed that in the absence of adjuvant, even two full doses of influenza vaccines were ineffective against a virus for which the human population was naïve. In marked contrast, a vaccine formulated with the MF59 adjuvant was very effective at inducing protective antibodies even with reduced dose. The trials repeated in 2005 and 2006 provided one of the most promising vaccines to the global vaccination against pandemic influenza. A letter published in *The New England Journal of Medicine* (Stephenson et al, 359:1631-1633, 2008) shows that any pandemic influenza caused by the virus H5 can be prevented by MF59-adjuvanted vaccine, independently of the virus used for vaccination.

A non-profit institute to develop vaccines against neglected diseases. In February 2008 there was the official opening of the Novartis Vaccines Institute for Global Health (NVGH) headed by Allan Saul. This Institute was entirely conceived and designed by me. The institute focuses on developing vaccines against neglected diseases. In 2015, as part of the GSK-Novartis deal, the institute acquired the name GSK Vaccines Institute for Global Health (GVGH). The institute has access to all technologies and know-how available at the GSK

Vaccines company. So far GVGH developed a conjugate vaccine for typhoid fever and is presently in clinical development with a Shigella vaccine supported by a grant from the Gates Foundation.

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 Giuliani, M. M. et al **Rappuoli, R. (corr author)**, and Pizza, M. (2006) A universal vaccine for serogroup B meningococcus. *Proc Natl Acad Sci USA* **103**, 10834-10839
- 15 **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
- 16 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
- 17 Scarselli, M. et al **Rappuoli, R.** (2011) Rational design of a meningococcal antigen inducing broad protective immunity. *Sci Trans Med* **3**, 91ra62
- 18 Black, S., De Gregorio, E., **Rappuoli, R** (2015) Developing vaccines for an aging population. *Sci Transl Med* **7**(281):281ps8
- 19 Bagnoli, F. et al **Rappuoli, R (corr. author)**, Grandi, G. (2015) Vaccine composition formulated with a novel TLR7-dependent adjuvant induces high and broad protection against *Staphylococcus aureus*. *Proc Natl Acad Sci U S A.* **112** (12):3680-5
- 20 Bloom, D.E., Black, S., Salisbury, D., **Rappuoli, R. (corr. author)** (2018). Antimicrobial resistance and the role of vaccines. *Proc Natl Acad Sci USA* **115**:12868-12871.
- 21 Andreano, E. et al **Rappuoli, R (corr. author)** (2020), Identification of neutralizing human monoclonal antibodies from Italian Covid-119 convalescent patients.

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