SPOTLIGHT ON VACCINES

Trends in vaccine development

How are public-private partnerships, low-cost manufacturers and new technology affecting the vaccine field?

"The vaccine field is going to enlarge substantially beyond the traditional preventive vaccine."

Rafi Ahmed, Emory Vaccine Center

BILL GATES is a handy person to have in your corner, which bodes well for those committed to vaccine research. In January 2010 the philanthropist called for a "decade of vaccines" and pledged US$10 billion for vaccine research and development (R&D) and distribution. The Bill & Melinda Gates Foundation funding will boost an already burgeoning field.

Although vaccines comprise a small portion of the global pharmaceutical market — 2 percent in 2010 — the industry is predicted to grow over the next few years. In the United States, demand will increase by around 7 percent annually until 2015, according to a 2011 report published by industry analysts Freedonia. "It's probably the best growth area right now in infectious disease," says Steve Projan, senior vice president of R&D in the innovative medicines unit at vaccine manufacturer MedImmune.

The industry is being shaped by increased collaboration between the public and private sectors, the rise of low-cost vaccine manufacturers and the use of new technologies. The changes are significant for those interested in working in the field.

IMAGE SOURCE

The three Ps

The expansion of public-private partnerships (PPPs) is "transforming the business of vaccines", says Gates. Although the model has been around since the early 1990s, it has taken time for vaccine research to be funded in this way. Camille Locht, director of the Centre for Infection and Immunity of Lille (CIIL) at the Institut Pasteur in Lille, France, says that five years ago the prevailing system in Europe was still that of competition between the public and private sectors. "Pharmaceutical companies have realized that for difficult diseases such as TB there will probably not be a single private or public entity that will come up with the final-stage vaccine," he says.

PPPs working in vaccines include the GAVI Alliance, the Aeras TB partnership and the International AIDS Vaccine Initiative (IAVI). CIIL is also a PPP, its partners comprising the Institut Pasteur in Lille — a private foundation — and the University of Lille, plus French public research institutes CNRS and INSERM. These meet needs not prioritised by the traditional vaccine development pipeline, with HIV a prime example. When the virus was identified in 1984, researchers were optimistic they could formulate a vaccine quickly. As HIV proved resilient, hopes for a fast response faded and by the early 1990s several research groups and companies had abandoned the search for a vaccine.

It became clear that a new model of vaccine development was needed, one that could bridge the gap between the public and private sectors and focus on the developing world. As a result, in 1996 IAVI was created with support from several foundations including the Rockefeller Foundation, plus the World Bank and other partners.

Established with just a handful of employees, IAVI now has 105 in-house research staff — around 75 percent of them with an industry background — and in April 2011 it launched a fellowship programme to recruit early-career postdocs from regions most affected by the HIV pandemic. It supports additional research staff through collaborations with more than 50 external partners and in February 2012 awarded US$875,000 to two researchers via open innovation broker NineSigma. IAVI's recent research advances include the 2009 discovery of two human antibodies that have a strong neutralizing effect on HIV, and the launch of two phase-one clinical trials of vaccine candidates in Africa in February 2011 and December 2011. The 2009 discovery was accomplished through a collaboration with the Scripps Research Institute in the United States and other international partners.

An early lesson for the initiative was the importance of recruiting experienced leaders and managers from the vaccine industry with proven project management skills. Vice president of vaccine development Thomas Hassell, who

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joined IAVI from Sanofi Pasteur in 2008, says getting the right people was important because PPPs generally lack the funds to support major training programmes. "As far as possible you want the finished product," he says. "You want people to get off to a racing start."

A major catalyst for the increased number of PPPs is the rising cost of early R&D as identifying new vaccine targets becomes more complicated. Vaccine manufacturers are turning to external collaborators for candidates. "Developing a vaccine today is much more complex than it was 20 or 30 years ago," explains Bruce Carpick, a biochemist in Sanofi Pasteur's analytical R&D arm in Toronto, Canada. "It's a natural progression for any major vaccine player to be looking to the external environment for opportunities." External collaborators also benefit from the arrangement as it can help their research reach the market, and many government funding schemes now offer incentives for working with industry. "It's a two-way street," says Carpick.

There is also increasing emphasis on safety and governance surrounding vaccines. "Regulatory requirements are much more stringent now than they were in the past," explains Carpick. "That has greatly increased complexity and cost."

For now substantial funding continues to emerge through the PPP model, despite the economic climate. Last year the GAVI Alliance secured a five-year pledge of US$4.3 billion from its donors, exceeding its target of US$3.7 billion, and in April 2011 the German Federal Ministry for Economic Cooperation and Development (BMZ) increased its contribution to the alliance by US$20 million, which the Gates Foundation matched. New PPPs are "definitely something you're going to see in the future," says Carpick.

Cut-price competition

The vaccine manufacturing industry has been transformed recently. Following 30 years of takeovers during which many independent vaccine manufacturers were bought out, new players are emerging. A significant trend is the growth of low-cost manufacturers in developing countries. Companies whose vaccines have been judged by the World Health Organisation (WHO) to meet international standards of quality, safety and efficacy — known as prequalification — include the Serum Institute of India; Bharat Biotech, Panacea Biotec and Shantha Biotechnics, also based in India; Bio-Manguinhos in Brazil; and Bio Farma in Indonesia. A cholera vaccine produced by Shantha Biotechnics is being used in a pilot programme to halt the spread of the disease in Haiti. In March 2011 WHO opened the way for vaccine manufacturers in China to submit products for prequalification after being satisfied that the country's regulatory systems were sufficiently robust. The decision coincided with news that Novartis Vaccines had bought a majority stake in Chinese vaccine manufacturer Zhejiang Tianyuan Bio-Pharmaceutical in order to expand its presence in China, the world's third-largest vaccines market.

Rafi Ahmed, director of the Emory Vaccine Center (EVC) at Emory University in the United States, says that manufacturers in India are providing a "tremendous" public health service by producing cut-price vaccines, but still need to build their R&D capabilities. He says these companies will need to collaborate more with research institutes in the United States and Europe as well as in India in order to make progress. To this end, last month India's Gennova Biopharmaceuticals opened a new vaccine-manufacturing facility in Pune in western India in partnership with two Seattle-based non-profit organizations, the Malaria Vaccine Initiative (MVI) and the Infectious Disease Research Institute (IDRI). Other recent developments that could increase Indian research capacity include the launch of Emory's Joint Vaccine Center with the International Center for Genetic Engineering and Biotechnology (ICGEB) in New Delhi, and the Hilleman Laboratories partnership between Merck and the Wellcome Trust, a US$145million not-for-profit initiative that will support 60 R&D staff.

Bring out the big guns

Immunology is often discussed in military-related metaphors, and this extends to the new technologies now available to vaccine researchers.

MedImmune headquarters in Gaithersburg, Maryland in the United States; the company is a leader in respiratory vaccines.

"Each scientific advance means a new weapon in the armament," says IAVI's Hassell. Since recombinant DNA vaccines emerged in the early 1980s, vaccine technology has diversified from culturing and attenuating whole microorganisms. One recent development is the boom in cheaper, faster DNA sequencing. "Genome-wide sequencing is a common tool now," says CIIL's Locht, explaining that the technology enables researchers to examine the effects of a vaccine at the genetic level.

As well as assessing efficacy, DNA sequencing can also be used to check vaccines for contamination with errant genetic material. Other technologies that have become integral to vaccine research include biochemical techniques such as protein purification and characterization, and improved assaying and imaging tools such as mass spectrometry, nuclear magnetic resonance (NMR) imaging and fluorescent tagging. "Vaccinology is very integrative," says Locht. Delivery technologies are another active area of research; Locht and his collaborators, for example, are developing a new pertussis (whooping cough) vaccine based on a single nasal dose of a live attenuated bacterium.

Despite recent advances, there is still significant potential for breakthroughs. "Immunology is a field in the dark ages," says MedImmune's Projan, emphasizing the need for improved *in vitro* and *in vivo* models for testing vaccines. Despite common perceptions, there isn't enough pharmacology expertise across the industry, he says.

There is a renewed focus on basic science to better understand the mechanism of vaccines and to develop new candidates, and an increasing interest in therapeutic vaccines for conditions such as chronic viral infections and cancer. "The vaccine field is going to enlarge substantially beyond the traditional preventive vaccine," says Ahmed of EVC. Bioinformatics and systems biology are also crucial aspects of future vaccine research.

At MedImmune, a leader in vaccines for respiratory diseases, valued skills include initiative and working under multiple managers. "It is increasingly complicated to discover, develop and commercialise [a new vaccine]," says Projan. "We can't rely on staid, formal, hierarchical reporting relationships."

And it is not just in R&D that jobs will expand. "You're also going to see opportunities in non-technical areas such as project management, regulatory affairs, clinical development and so forth," says Carpick.

Two years into Bill Gates's decade of vaccines, there is much optimism and potential for stimulating opportunities for scientists with the right skills. "It's one of the most exciting areas of science right now," says Ahmed. ■

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Else Kröner Fresenius Immunology Award
Call for Candidates

In commemoration of the 25th anniversary of the early death of Else Kröner, June 5, 2013, the Else Kröner-Fresenius-Stiftung (Foundation) intends to award world-wide pioneering discoveries in the field of medical immunology and to facilitate future research by the winning individual or team.

The award - At least 500,000 € will be awarded to the winner(s) in person. Up to 3,500,000 € will be awarded for future research.

The candidates must be fully active researchers, who have made groundbreaking discoveries in medical immunology. They need to be in the position to accomplish the research intended in the next 3-5 years.

Candidate nomination - Candidates will be proposed by IUIS member associations. Self-nominations need to be accompanied by two letters of recommendation from at least two internationally leading researchers in immunology from two different countries.

Deadline for nominations: July 4, 2012. For further details please see www.ekfs.de and www.iuisonline.org.

ELSE KRÖNER-FRESENIUS-STIFTUNG

IUIS international union of immunological societies

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FAU FRIEDRICH-ALEXANDER UNIVERSITÄT ERLANGEN-NÜRNBERG
MEDIZINISCHE FAKULTÄT

The Faculty of Medicine at the Universität Erlangen-Nürnberg, Department of Dermatology invites applications for a

W2-Professorship for Tumor Immunology with focus on systems biology

A fixed-term professorship with the status of a civil servant is available for a total of six years.

The successful candidate is expected to represent the field in research and teaching at the university. We are looking for a candidate with expertise in the field of bioinformatics and systems biology approaches. The biological focus of the work will be the identification of predictive signatures and molecular mechanisms relevant for immunotherapy. Cooperation with other research groups particularly of the Faculty of Medicine is expected. The Faculty of Medicine offers study programs in Medicine and Dentistry, a Bachelor/Master program in Molecular Medicine and a Master program in Medical Process Management.

Prerequisites for employment are a university doctoral degree, teaching skills and scientific achievements including successful grant applications and publications in peer-reviewed journals. Preferably, the latter is documented by a "habilitation", a previous junior faculty position or by equivalent appointments and positions outside academia. The successful candidate will be expected to take over administrative duties and also to attract external funding.

The Universität Erlangen-Nürnberg is an Equal Opportunities Employer. With respect to further preconditions for the job, legal provisions apply. Further information can be found on:
http://www.uni-erlangen.de/infocenter/jobs/professoren/Tumor-Immunology.shtml

Please submit your application and the supportive documents (curriculum vitae in tabular form; list of publications subdivided in original papers, review articles and book chapters; a list of research grants and teaching activities; officially certified copies of your credentials and certificates) in written as well as digital form (on CD-ROM or per E-mail) to the Dean of the Faculty of Medicine at the Universität Erlangen-Nürnberg, Östliche Stadtmauerstr. 30a, 91054 Erlangen, Germany. For more information please visit our website at http://www.dekanat.med.uni-erlangen.de. The deadline for application is **8th June 2012**.

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UNIVERSITÉ DE STRASBOURG

Postdoctoral Position
PhD Student Position

Inserm Virology Unit, Laboratory of Excellence HEPSYS, University of Strasbourg, France

A postdoctoral position and a PhD student position are open in the Inserm Virology Unit U748 and the Laboratory of Excellence HEPSYS (Head and Director: Prof. Thomas F. Baumert) at the Institute of Virology, University of Strasbourg, France. The unit and laboratory is located in an excellent infrastructure of the Institute of Virology on the campus of the University of Strasbourg in an outstanding scientific environment. A state of-the-art BSL3 laboratory, advanced imaging and flow cytometry platforms are on site.

The unit program is focused on the study of the molecular mechanisms of virus-host interactions and the development of novel antivirals and vaccines (see Lupberger, Zeisel et al. Nature Medicine 2011, Fafi-Kremer et al. J. Exp. Med. 2010, Fofana et al. Gastroenterology 2010, Lambotin et al. J. Virol. 2010, Lambotin et al. Nature Rev. Microbiol. 2010, Benga et al. Hepatology 2010; Dimitrova et al. PNAS 2008, Barth et al J. Virol 2008; Pestka et al. PNAS 2007).

The successful candidates will have strong background in molecular biology, virology, immunology or cancer research. We are looking for one applicant to investigate the molecular mechanisms of viral entry and immune evasion and one applicant for the study of the molecular mechanisms of virus-induced cancer. The successful candidates will join a well-funded international and young research team in an outstanding scientific environment (Laboratory of excellence HEPSYS, University of Strasbourg) including established partnerships with the pharmaceutical industry. Medical doctors with a strong interest in a career in translational research are also encouraged to apply. While knowledge of the French language is not required, English proficiency is mandatory and strong communication and organization skills are expected.

Successful candidates will have the opportunity to enter the Inserm and University of Strasbourg tenure track programs.

Please send your CV (including experience, publications and academic references) and a brief statement of research interests to:
Prof. Thomas Baumert and Dr. Mirjam Zeisel, Inserm U748, 3 rue Koeberlé, F-67000 Strasbourg, France. E-mail: Thomas.Baumert@unistra.fr and Mirjam.Zeisel@unistra.fr

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UMASS University of Massachusetts Medical School

Faculty Position in Innate Immunity

UMMS is located within a 67-acre integrated health science campus, encompassing the School of Medicine, Graduate School of Biomedical Sciences, and Graduate School of Nursing, located in the picturesque Worcester Hills/Lake Quinsigamond region of central Massachusetts. The Division of Infectious Disease and Immunology has a major focus on innate immunity, autoimmunity and host-microbe interactions, utilizing human, murine and invertebrate models and coordinates research activities of the recently formed Institute for Innate Immunity.

We are currently recruiting for a full-time tenure-track faculty position.

Appointed rank will be commensurate with experience. Faculty at UMMS engage in teaching, research and service, and successful candidates will be expected to direct an externally funded independent research program as well as participate in graduate education. Laboratory space and extensive core facilities are available in the recently constructed Lazare Research Building. Candidates must have a Ph.D. and/or M.D. (or equivalents), and a record of significant research accomplishments in any area of innate immunity. Highest priority will be given to investigators with outstanding research programs that complement our current strengths. Successful candidates will also demonstrate strong communication skills and an interest in collaborative research endeavors. Review of applications will begin on April 15th, 2012 and will continue until the position is filled.

Applicants should upload a cover letter, CV, research statement and publication list to https://academicjobsonline.org/ajo/jobs/1498. To expedite the review process, applicants should also invite three individuals who are familiar with their work and potential for success to upload recommendation letters to http://www.academicjobsonline.org. Please refer any questions regarding the search to: Neal Silverman, Search Committee Chair and Professor of Medicine, neal.silverman@umassmed.edu

As an equal opportunity and affirmative action employer, UMMS recognizes the power of a diverse community and encourages applications from individuals with varied experiences, perspectives and backgrounds.

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HIV Research Faculty Position

The University of Michigan Department of Medicine, Division of Infectious Diseases seeks M.D. candidates board certified (or eligible) in Infectious Diseases for tenure-track positions at the Assistant, Associate, or Full Professor rank to develop and conduct independently funded **basic and/or translational research programs relevant to HIV.** Investigators will join a growing and interactive group of researchers with close ties to both basic science and clinical departments within the University, and the potential for joint appointments within graduate departments of the University of Michigan. Interested individuals should submit *curriculum vitae*, summary of research and career goals for junior applicants, and contact information along with three references addressed to:

David M. Aronoff, M.D.,
Search Committee Chair
Division of Infectious Diseases
Department of Internal Medicine
c/o Carly Kish
1500 E. Medical Center Drive
3119 Taubman Center/SPC 5378
Ann Arbor, MI 48109-5378
Or email: ckish@med.umich.edu

The University of Michigan is an Equal Opportunity Employer; women and minorities are encouraged to apply.

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National Cancer Institute

Frontiers in Basic Immunology: 2012

October 4-5, 2012
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The meeting will include sessions on lymphocyte biology and signaling, adaptive and innate immune responses, and immunity and disease

Registration is now open and abstracts are being accepted for the poster session. Deadline for abstract submission is August 17, 2012. Register online:

http://web.ncifcrf.gov/events/Immunology2012

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