

SPOTLIGHT ON CANCER RESEARCH

Cutting-edge therapy builds on an age-old discovery

The growing field of immunotherapy is looking for new ways to employ the body's immune system in the fight against cancer

"The field has evolved to the point where you're on the horizon of making a large impact."

Robert Abraham, chief scientific officer, Pfizer Oncology Research Unit

A HUNDRED and fifty years ago a New York doctor, William Coley, read about a patient whose bone cancer vanished after a high fever. Coley wondered whether there was a link between the fever and the cancer remission, and began intentionally injecting bacteria into the tumors of his patients to give them severe infections. His unorthodox methods worked, and Coley successfully treated hundreds of cancer patients, despite never quite understanding why.

Now scientists have figured out why Coley's technique had such significant effects, and are developing his idea to come up with revolutionary advances in cancer therapy. The germ of Coley's success came from a concept now termed cancer immunotherapy – coaxing the body's own immune system into fighting the disease. Scientists have known for decades that cancer cells are exceptionally effective at evading the body's natural immune response, which is why most treatments employ other ways to destroy or remove cancerous cells, such as radiation therapy, surgery and chemotherapy.

But by increasing the production of immune cells and molecules, engineering immune cells to recognize tumors as foreign, or preventing tumors from blocking the immune system, researchers initially shrunk or eliminated tumors in mice. Over the past five years, those advances have been applied to human patients, with large clinical trials on immunotherapy agents showing positive against blood, skin, breast, lung, and other cancers. The approach not only offers hope of curing cancer, but of causing fewer systemic side effects than conventional chemotherapies, meaning a new set of opportunities for cancer researchers looking to impact on patients' lives.

Immunotherapies comprise antibodies, which directly attack cancer cells; vaccines, which spur the body to make its own antibodies; and drugs that promote general activity of the immune system. Today, immunotherapy-based approaches are used in about three percent of cancer patients, but a recent report by Citigroup concluded that in the next decade, immunotherapy will become the cornerstone of treatment in up to 60% of cancer cases and the industry will reap up to US\$35 billion per year.

For basic biologists, immunologists, oncologists, and pharmaceutical chemists, the field of immunotherapy is rich in research and development opportunities. "Immuno-oncology is a really up and coming field, especially in light of some of the successes we have already seen this decade," says Helen Sabzevari, senior vice-president of Immuno-Oncology at the pharmaceutical company EMD Serono.

However, there are important unanswered questions about how to optimize immunotherapy techniques, says Richard Vile, an immunologist at the Mayo Clinic in Rochester, Minnesota, whose team specializes in experimental cancer therapies based on the immune

system. These questions represent new challenges for those entering the field. "The more we understand the details of the immune system and its interactions with tumors, the more we find out we don't yet know."

Immunological mimicry

From William Coley's day firmly into the twentieth century, attempts at immunotherapy hinged on the general principle that any increase in the immune system's activity helped the body fight cancers. But as the basic science of immunology has matured, the approach has become more detailed. "Immunotherapy is evolving from a very broad brush to actually targeting very specific pathways," says Vile. "The individual molecules involved are better understood than ever before, and the challenge for the next few years is understanding how all those pathways truly interact and how to apply that knowledge to the clinic."

One development has been to make antibodies in the lab which mimic the desired action of the immune system. For instance, tumor cells can avoid the immune system by mounting a protein called PDL1 on their outer surface, which shields them against T-cells – the primary immune response to a tumor. PDL1 sticks to a protein on the surface of T-cells called PD1,



Located in Tampa, Florida, Moffitt Cancer Center has over 4,200 employees and contributes nearly US\$2bn annually to the economy of the state.

an interaction which 'shuts down' the T-cell and protects the tumor.

At Fred Hutchinson Cancer Research Center in Seattle, Washington, oncologist Mac Cheever leads the Cancer Immunotherapy Trials Network (CITN). Cheever has been involved in immunotherapy since the 1970s, when clinicians observed that cancer patients who developed an immune response following a bone marrow transplant recovered from leukemia better than those whose immune system did not respond. The National Cancer Institute-funded network of researchers from 29 institutions is collaborating to move selected immunotherapies from the lab to clinical trials. One such therapy uses a monoclonal antibody called anti-PD1, which itself binds to PD1, blocking the cancer cell from doing so and therefore lifting the brakes on T-cell proliferation.

Trials have so far shown anti-PD1 to have an impact on 30 percent of melanomas, and around 20 percent of lung cancers. The lung cancer results are particularly exciting, Cheever says, as "lung cancer was not felt to be an immune responsive tumor". "I would predict going forward just three or four years, almost every patient will be evaluated to see if they'll respond to anti-PD1 drugs," he adds.

Despite the progress, establishing how to evoke a response in the other 80 percent of patients, using other immunotherapies or combinations of drugs, remains one of the big challenges in the field.

Researchers at Pfizer's oncology research unit around the US are trying to work out why some patients naturally develop T-cells that recognize a cancer, and others don't, and why immunotherapy drugs work better

Making it personal

In the 10 years that immunotherapy has evolved to bring real clinical applications, another field has had a large impact on the study of cancer biology. Genomics and high-throughput genetic sequencing technologies have gained importance as tools in cancer research and now the two fields are coming together.

"It's become apparent not all patients respond to even these drugs we're excited about," says Pfizer's Robert Abraham. For scientists with a background in the genetics of cancer, and an interest in immunology, the questions of why some people respond differently to immunotherapies is ripe for study. Their findings—if they can link the genetics of a cancer to the success rate of immune-based drugs—may not only lead to a better understanding of the biology of tumor immune responses, but better, more targeted, care for patients.

Richard Vile says there is a huge increase, particularly in the genomics field, in interest in combining immunotherapy with the idea of personalized or individualized medicine.



Researchers at EMD Serono are working on cancer vaccines using immunotherapy.

in some people than others.

In spite of stigma due to early failures, another avenue that offers much potential is cancer vaccines, says Sabzevari. "I think this field is just getting started and we will see a lot of successes in the coming years," she says.

Answering these questions means straddling the intersection between basic science and patient data. The immune system is complex, says Robert Abraham, chief scientific officer at Pfizer's Oncology Research Unit in New York, "and when you intertwine that with tumor biology, the complexity becomes quite daunting." Abraham says these challenges are what make it such an invigorating field of research for young scientists to pursue.

Diversity pays

The future success of the field relies on co-operation between scientists in academia and industry, says Sabzevari. "When I was at

graduate school there was always this concept of academia versus pharma and I think the time has come to completely break down these barriers," she adds.

The best advances will also come from a mix of backgrounds, says Vile. "The beauty of immunology is that it really touches so many other fields—molecular biology and biochemistry can easily be applied to what we're studying. When you have people coming in from different fields they build up their own views and look at the problems from a new angle."

Sabzevari's research background is in oncology and immunology, and she says this is an exciting time for scientists with that breadth of expertise. "Individuals with a good understanding of cancer biology and a solid training in immunology can see the biggest picture, and apply it," she says.

Abraham says the greatest demand is for scientists with

specific training in immunology, immunobiology, and T-cell biology.

According to tumor immunologist Jeffrey Weber, director of the Donald A. Adam Comprehensive Melanoma Research Center at the Moffitt Cancer Center in Tampa, Florida, resilience is also vital. "To succeed in this field you need to accept the fact that you're going to fail most of the time and not get discouraged by that. You need to be incredibly stubborn."

Weber encourages young scientists interested in immunotherapy to pursue a joint MD/PhD course of study, which can prepare them for the balance of clinical skills and basic research know-how that the career requires. "I'd encourage people at the get-go to start working in a lab. A few will survive and those are the people who have the potential to be great scientists."

The key is a genuine interest in immunology, says cellular immunologist Hans-Reimer Rodewald, who warns against entering the field for the wrong reasons: "I don't think it's a good idea to jump into the field just because it's hot."

Rodewald received his PhD from the Max-Planck Institute of Immunobiology in 1988 and now works at the German Cancer Research Center (DKFZ) in Heidelberg. There he is trying to understand how to better model the interaction between the immune system and tumors in mice. As a basic scientist, the clinical implications may seem far removed from his work, but for Rodewald the excitement is in answering scientific questions. Immunotherapy, he adds, is "a great field and a young field."

For others, such as Abraham, it's the clinical applications that are the most rewarding, and which seemed outside the realm of possibility when he was working as a bench scientist in immunology. "Back then, clinical applications in oncology seemed so far away. As you were working in the lab, you didn't have any sense that what you were studying could be helping patients," he says. "Now the field has evolved to the point where you're on the horizon of making a large impact." Or as Weber puts it: "It's a good time to be in the field, and the best is yet to come."

Nature editorial staff have no responsibility for content



Work in Moffitt's basic science laboratories includes immunotherapy research.



THE FIRC INSTITUTE OF MOLECULAR ONCOLOGY
MILAN - ITALY

THE INSTITUTE FOR STEM CELL RESEARCH
AND REGENERATIVE MEDICINE AND
THE NATIONAL CENTRE FOR BIOLOGICAL SCIENCES
BANGALORE - INDIA

Independent International Research Position in “Molecular and Cellular Basis for Tissue Homeostasis and Inflammation”

Applications are sought for a joint PI position between the FIRC Institute of Molecular Oncology (IFOM), Milan, Italy - <http://www.ifom.eu/en>, the Institute for Stem Cell Biology and Regenerative Medicine (inStem) - <http://instem.res.in> and the National Centre for Biological Sciences (NCBS) - <http://ncbs.res.in>, Bangalore - India. As part of the continuing expansion of this institutional partnership, the PI will be a member of the “IFOM-inStem Joint Centre for Tissue Homeostasis and Inflammation”. This junior group leader position will be based in Milan to establish a research program at the forefront of stem cell biology.

Current projects at the Joint Centre focus on the study of epithelial homeostasis and immune regulation at barrier surfaces, and the regulation of progenitor cells in a wound-healing microenvironment. Candidates pursuing an exciting program in any field of stem cell biology who can interface with the programs at the Joint Centre at inStem will be considered. Research programs may include - but are not limited to - the regulation of stem cell behavior, biogenesis and maintenance of cancer stem cells and tumor-stroma interactions.

The position will be based at IFOM, Milan and will involve active membership of the Joint Centre in Bangalore through regular visits and collaborative projects. The successful candidate will have an attractive salary, generous laboratory space, full access to world-class facilities, and access to excellent graduate students and postdoctoral fellows from both IFOM and inStem.

Candidates should have a PhD, postdoctoral experience with an outstanding research record in the field of stem cell biology, the potential to establish an internationally competitive research program, commitment to mentor graduate students and postdoctoral fellows, and the ability to attract research funding.

Application materials should include:

- A CV with a list of publications in international peer reviewed scientific journals
- A summary of the past and current research interests (up to 2 pages)
- A description of the proposed research (5 pages maximum)
- The names and contact information of at least 3 scientists from whom letters of recommendation can be requested.

To ensure full consideration, these documents should be sent as a PDF file to the following e-mail address: ncbs-team@ifom.eu by **October 30th 2013**.

Selected candidates will be invited to visit both Milan and Bangalore Institutes for direct interviews.

W240765R



Director, Pediatric Molecular Oncology Program Penn State Hershey Children's Hospital Pennsylvania State University College of Medicine

The Division of Pediatric Hematology/Oncology at the Penn State Hershey Children's Hospital is recruiting a director for the newly established Pediatric Molecular Oncology Program. This Program is supported by a \$20 M endowment from the Four Diamonds Fund of the PSU College of Medicine, part of a \$50 M endowment supporting the Four Diamonds Pediatric Cancer Research Program. The mission of the Pediatric Molecular Oncology Program is to understand tumor development at a molecular level and to develop genetic and proteomics analysis of pediatric cancers to individualize selection of therapy. This will include support for basic and translational research studies and/or clinical trials. Rank is at the Associate to Full Professor level commensurate with the applicant's experience and accomplishments. Successful applicants will have an M.D./Ph.D., Ph.D., or M.D. degree with an established track record in cancer research and demonstrated ability to obtain extramural funding (R01-type award).

The Division of Pediatric Hematology/Oncology has 11 full-time Pediatric Hematologists/Oncologists and 6 Ph.D. faculty. Over 100 new oncology patients are seen annually, and there are programs in pediatric stem cell transplantation, neuro-oncology, survivorship, hemophilia, and sickle cell disease. The division has an accredited Pediatric Heme/Onc fellowship program and is an active member of COG and POETIC. The Four Diamonds Pediatric Cancer Research Program includes NIH-funded basic science and translational research in transcriptional and epigenetic changes in leukemia and solid tumors. Research is supported by the Penn State Cancer Institute, the Penn State Hershey Institute for Personalized Medicine, an NIH-funded CTSA, and Pediatric Clinical Trials Office. Basic core, translational, and clinical facilities provide an excellent environment for research.

Please submit a current CV and letter of interest to: Barbara Miller, M.D. (bmiller3@psu.edu), Chief, Division of Pediatric Hematology/Oncology, Penn State Children's Hospital, the Pennsylvania State University College of Medicine, Box 850, MC H085, Hershey, Pennsylvania 17033. Applications are accepted until position filled.

Penn State Milton S. Hershey Medical Center and the College of Medicine are Equal Opportunity/Affirmative Action employers and encourage applications from women and members of minority groups.

NW240907R



SCIENTIFIC PROGRAM LEADER Associate/Full Professor (tenure eligible) Position Number: F35670

Hire Date: January 1, 2014

Deadline: Open until Filled

The Massey Cancer Center of Virginia Commonwealth University (VCU), an NCI-designated Cancer Center and VCU School of Medicine are recruiting a senior scientist to lead its Radiation Biology and Oncology (RBO) Scientific Program. One of five scientific programs with the Massey Cancer Center, and one of only nine programs in NCI-designated Cancer Centers in the country with an emphasis on radiation sciences, the RBO has a scientific focus in the areas of DNA repair, tumor microenvironment, and the impact of inflammation on tumor radio responsiveness and normal tissue radio sensitivity. The RBO program also is one of the only two programs in the Cancer Center with an active clinical trial component. A multidisciplinary program with sixteen members representing four different departments and two schools, membership in the RBO consists of five laboratory scientists, three medical physicists, one biostatistician and seven clinicians.

This is a tenure-track appointment at the rank of Associate Professor or Professor in the VCU School of Medicine, commensurate with the candidate's experience. The successful candidate will have a track record of sustained extramural funding, publication and recognition as a leader in his/her field of study. He/she will be expected to provide scientific direction, foster inter- and intra-programmatic collaborations leading to growth of the program, and expand the program's translational research component. He/she must have a Ph.D. and/or M.D. in a relevant scientific area. The successful candidate must have demonstrated experience working in and fostering a diverse faculty, staff, and student environment or commitment to do so as a faculty member at VCU. Richmond is a mid-sized metropolitan area with close proximity to Washington, D.C., the beautiful Blue Ridge Mountains, and scenic coastal areas.

For further details, please contact: Donna Berrier; Phone: **804-628-1322**; email: dberrier@vcu.edu. Applications shall be forwarded to: **Donna Berrier, CAO, VCU Massey Cancer Center, 401 College Street, P.O. Box 980037, Richmond, VA 23298-5083** or email at dberrier@vcu.edu.

Virginia Commonwealth University is an equal opportunity/affirmative action employer. Women, minorities, and persons with disabilities are encouraged to apply.

NW241738R



The Francis Crick Institute

<http://www.crick.ac.uk>

The Francis Crick Institute will open at St Pancras in central London in 2015. Its research will use interdisciplinary approaches to investigate the biology of human health and disease, supported by core funding from CRUK, the MRC, and the Wellcome Trust, and by grants from UK and international funding agencies.

The Crick is expanding Computational Biology research as a key component of its scientific strategy. The institute will offer an outstanding environment for computational research, with excellent opportunities for wet/dry collaborations across the range of biomedical and clinical research disciplines, supported by a strategic alliance with the Wellcome Trust Sanger Institute. The new Crick laboratories will feature excellent computational facilities including a state-of-the-art data centre.

The London Research Institute

<http://www.london-research-institute.org.uk>

The London Research Institute (LRI) is the largest Cancer Research UK research institute, with 40 research groups focusing on fundamental cancer biology. The Institute is based in well-equipped laboratories at Lincoln's Inn Fields in central London, and at Clare Hall in Hertfordshire.

The LRI recruitment process for 2013 will be carried out jointly with the Crick Institute. We shall appoint outstanding scientists seeking to establish independent and innovative research programmes focussed on:

Computational Biology in Cancer

using approaches such as **Bioinformatics, genomics, systems biology, mathematical modelling, image analysis**

Informal enquiries may be made by e-mail to Nicholas.Luscombe@cancer.org.uk

Newly appointed group leaders will receive core funding for research personnel, travel and consumables, and access to the Institute's comprehensive computational core facilities, backed by competitive employment terms. The new group leaders will move to the Crick laboratories in 2015.

Applications should include the following files, in .pdf format, and should be submitted online at <https://lrigroupleader.cancerresearchuk.org>

1. Complete CV
2. Publication List (please separate primary papers and review material)
3. Long-term vision for your research programme (approx 500 words)
4. Past and Future research plans (approx 2000 words)
5. Names and contacts of at least 3 academic referees

YOUR REFEREES will be instructed to submit letters of recommendation online at the time the application is received.

APPLICATION DEADLINE: November 22nd 2013

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Faculty Positions in Cancer Biology and Immunology at the Vaccine & Gene Therapy Institute of Florida

The Vaccine & Gene Therapy Institute of Florida (VGTI Florida) is recruiting outstanding immunologists to establish research laboratories in basic and translational cancer immunology. The important targeted areas of research include immune-based personalized therapeutics development, adoptive T cell therapies, antibody-based strategies, innovative immune monitoring approaches and vaccine development. Priority will be given initially to established investigators with vigorous research programs investigating cancer vaccines, tumor microenvironment and cell-based immunotherapy. VGTI Florida is one of the internationally recognized research institutes invited to locate to Florida as part of a State-sponsored initiative to enhance biomedical research. Research at VGTI Florida focuses on human innate and adaptive immune response to infectious diseases and cancer.

Research themes of VGTI Florida include:

- Cancer Immunology and immunotherapy
- HIV-1 and emerging viral pathogens
- Vaccine development and adjuvants
- Inflammation and diseases of aging

VGTI Florida occupies a new 100,000 sq. ft. state-of-the-art facility in Port St. Lucie, FL, located on the sunny Atlantic coast in a Biotech corridor just north of Palm Beach. Successful candidates (PhD and/or MD) will have a robust extramurally-funded research program and a strong publication record in one of the priority areas described above. The positions have highly competitive salary and startup packages, with access to cutting edge Genomics, Bioinformatics and Flow Cytometry core facilities as well as BSL3/ABSL3 containment facilities within the Institute. For more information, including a description of the Faculty and their research interests, please visit: www.vgtifl.org. Qualified candidates should submit their curriculum vitae, a 2-page description of their proposed research program and the names/contact information of three references by email to:

Jill Hackett
Executive Director, Human Resources

The email address is search@vgtifl.org. Review of applications will commence immediately, and continue until the positions are filled. VGTI Florida is an Equal Opportunity Institution committed to recruiting, hiring, and promoting qualified minorities, women, individuals with disabilities, and veterans.

NW241678R

Assistant or Associate Professor



The Department of Cancer Biology at the Perelman School of Medicine at the University of Pennsylvania seeks candidates for an Assistant, Associate, and/or Full Professor position in the tenure track. Rank will be commensurate with experience. The successful applicant will have experience in the field of cancer biology, including but not limited to cancer genetics and genomics, tumor microenvironment, chromosome biology, cancer cell metabolism and oncogenic signaling.

Responsibilities include the development of an independent research program. Teaching duties comprise mentoring students and course lecturing. Applicants must have an M.D. and/or Ph.D degree and have demonstrated excellent qualifications in education and research.

We seek candidates who embrace and reflect diversity in the broadest sense. The University of Pennsylvania is an equal opportunity, affirmative action employer.

Apply for this position online at: http://www.med.upenn.edu/apps/faculty_ad/index.php/g304/d3418

NW241517R



UNC
LINEBERGER

The UNC Lineberger Comprehensive Cancer Center, in collaboration with departments in the UNC Chapel Hill School of Medicine, seeks outstanding candidates for multiple faculty positions at all levels and at all ranks to expand our tumor immunology / immunotherapy program. These positions coincide with development of a GMP facility for delivering novel immune-based approaches to treat patients with cancer. This broad-based recruitment seeks candidates in all areas of tumor immunology research; however, applicants should have a track record of clinical/translational or basic research focused on enhancing the adaptive and/or innate immune response for the treatment of specific malignant diseases. Applicants should also have a strong record of recent accomplishments as a post-doctoral fellow or sustained productivity as an established faculty member. Appointment and rank in an academic department will be determined by the applicant's qualifications. Faculty are expected to compete for extramural funding from the National Institutes of Health and other agencies. Applications will be reviewed beginning December 1, 2013 and until the positions are filled.

Educational Requirements: Doctoral Degree

Qualifications and Experience: Doctoral Degree

Apply online at <http://unc.peopleadmin.com/postings/32265>. Please provide a CV, a research statement, and a list of four references.

The University of North Carolina at Chapel Hill is an Equal Opportunity Employer. Women and minorities are strongly encouraged to apply and self-identify on their application.

NW241427R

FACULTY OF MEDICINE INVITES APPLICATIONS FOR FOLLOWING POSITION

Professor in Autoimmune Diseases, especially Diabetes and Coeliac

FACULTY OF MEDICINE

The Department of Clinical Research Sciences, Malmö

Application deadline 14 november 2013, ref nr PA 2013/248



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www.lunduniversity.lu.se/jobs

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Group Leader Positions

Cancer Research UK Cambridge Institute, University of Cambridge

Salary range £37,382 to £98,900 depending on experience, with a supplement potentially available for outstanding candidates.

The Cancer Research UK Cambridge Institute (www.cruk.cam.ac.uk) at the University of Cambridge receives generous core funding from Europe's top cancer charity, Cancer Research UK. Since it opened in 2007 the Institute has established a reputation for international excellence in cancer research. Situated on the Cambridge Biomedical Campus adjacent to other world-class research laboratories and Addenbrooke's Hospital, the Institute works closely with clinicians and researchers in many disciplines from across the University, local institutes and biotech.

The Institute's research ranges from basic experimental and computational cancer biology through translational cancer research to clinical application. The Institute currently houses over 350 researchers and support staff with 20 research groups and associated core facilities in a state-of-the-art research facility. Following the appointment of the new Director, Professor Simon Tavaré FRS, the Institute will add a further 10 research groups and open up extensive new laboratory space in the next step of a phased expansion.

We are looking for Junior and Senior Group Leaders with outstanding track records to develop a set of integrated scientific programmes with particular emphasis in:

- Bioinformatics, computational biology, cancer systems biology, statistics, image analysis;
- Experimental medicine;
- The epithelial biology of hormone-driven cancers;
- In vivo models and imaging;
- The biology of preneoplasia and early detection.

We are particularly interested in cancers of unmet need (e.g. glioblastoma, oesophagus, lung and pancreas), and we wish to recruit both clinical and non-clinical scientists.

Successful applicants will be expected to lead an independent research programme that contributes to the overall goals of the Institute. All posts carry a significant core package of salaries and support.

For further information and details on how to apply please go to <http://www.jobs.cam.ac.uk/job/2186/>

There is no closing date. Applications will be assessed continuously throughout the year.

The University values diversity and is committed to equality of opportunity.

www.jobs.cam.ac.uk

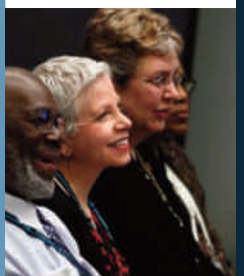
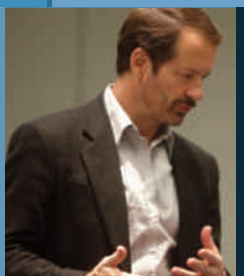
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