SPOTLIGHT ON CANCER RESEARCH

# Cancer genomics: Collaborative research

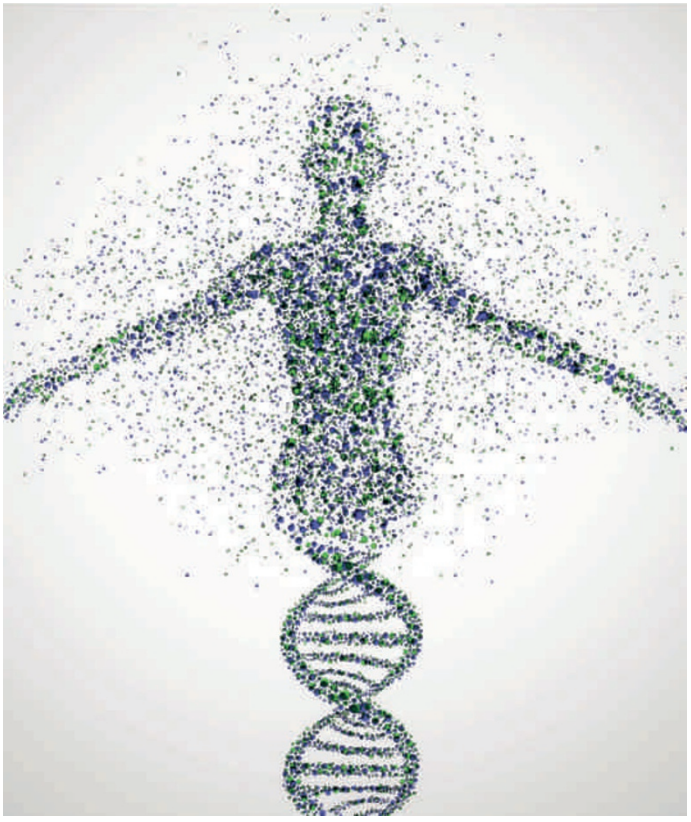
As sequencing costs reduce and computing power expands, opportunities abound for scientists to learn about the genetics of cancer.

*"You don't have to wait for another Large Hadron Collider to be built to answer questions in this field."*

*Andrea Sottoriva, London's Institute of Cancer Research*

**WHEN ROBERT** Strausberg started his career in 1976 as a microbiologist, studying yeast as a postdoc at Southwestern Medical School, he had no idea that one day he'd be working in cancer genomics

From a field that did not exist, it has become a promising new direction for understanding and treating cancer, attracting researchers from across scientific disciplines, some of whose expertise might not have seemed immediately useful for cancer research. "I didn't think what I was doing applied to much else," says Strausberg, now executive director of collaborative sciences at Ludwig Cancer Research in New York. But it turned out his experience was more useful than he thought. An early-stage biotechnology company, Genex, hired him to apply his knowledge of yeast to develop vaccines and drugs. His studies of yeast's mitochondrial DNA and what he'd learned about the physical mapping of DNA eventually won him the head role at the Sequencing Technology Branch at the US National Center for Human Genome Research among various other jobs at the National Institutes of Health. Because genomics is basic to biology, Strausberg's increasing knowledge helps him understand various fields important to human health, from infectious disease to agriculture. "My interest in genomics has opened a lot of doors for me."



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Genomics is the study of the set of genes within an organism. As gene sequencing costs decrease and computing power continues to grow, it's become possible to collect and analyze the information contained within a genome. In cancer, that translates to figuring out which mutations are involved — not only by cancer type but by individual patient. Researchers are learning about the causes and progression of tumour evolution, identifying targets for therapy, and seeing which genes may make a particular drug more or less likely to be effective.

Genomics is increasingly being applied to the clinical treatment of cancer, as well as to research into cancer biology. It also contributes to targeted cancer therapy, where treatments are aimed at specific genes or mutations in a particular patient. This approach can prove more effective and less toxic than traditional chemotherapy, which kills cells indiscriminately. "Cancer genomics for me is an opportunity to develop new treatments for advanced cancers, to learn how the disease develops in the first place, to do better detection and prevention," Strausberg says. "To me having a specialty in genomics gives one a very broad field of opportunity."

There's plenty of funding for the field too. In the US, the National Cancer Institute has created the Cancer Genome Atlas, which is collecting genomic information about more than 20 different types of cancer and making them available to researchers for analysis. The US National Human Genome Research Institute collects genetic research on several types of cancer and provides funding for university scientists. Cancer Research UK has created a multidisciplinary project award to encourage research by multi-discipline teams and plans to fund about 10 projects with up to £500,000 over four years.

## Varied expertise

Cancer genomics exists at the intersection of clinical work, biological research and computer science. Therefore, there's a need for researchers from various

disciplines – medicine, molecular biology, chemistry, computational modeling, bioinformatics, mathematics, even engineering and physics. Whatever their speciality, scientists entering the field need to be conversant with other disciplines and be comfortable working with researchers from different areas. "You actually need specialists from different fields working together to understand what is going on," says Moritz Kircher, who is both a clinical radiologist and a researcher in molecular imaging at Memorial Sloan Kettering Cancer Center in New York. "No-one can alone really tackle those questions anymore."

Kircher works in radiogenomics, attempting to correlate information from imaging techniques such as magnetic resonance imaging with sequenced genes. If specific genes have specific effects on the image of a tumour, doctors might get a better idea of what's happening with a cancer overall, and progressively, than they would from taking a biopsy from only a small area of the tumour.

Kircher's also developing nanoparticles that use the signatures of genetic mutations to home in on tumour cells and let pathologists image more detailed information. His lab, for instance, recently developed Raman nanostars, tiny, star-shaped gold particles coated in silica that shine brightly under laser light. Early tests on mice showed the nanostars could detect tumours as small as 100 microns, as well as premalignant lesions.

In the UK there's a shortage of people able to maintain the datasets and analyze the sequencing data being produced, says Ultan McDermott, a team leader in the Cancer Genome Project at the Wellcome Trust Sanger Institute in Hinxton. A lot of the initial work that used sequencing data from a few dozen or a few hundred samples to create and validate algorithms is done. The challenge now, McDermott says, is to scale up the algorithms so they can work with hundreds of thousands of samples, and to make sure people from outside the group that developed the programs can make use of them. "Developing these is going to be a lot of work and hugely important," McDermott says.

## Much depth, some breadth

It's a good idea, researchers say, for people from one scientific discipline to have some understanding of others they'll be dealing with in genomics research. Biologists entering the field should have some grounding in statistical analysis and some sense of how computational modeling works in order to make sense of the quantitative data they're looking at. "I wouldn't suggest medical doctors or molecular biologists start doing a whole course on computational models or bioinformatics," says Andrea Sottoriva, head of the Evolutionary Genomics and Modelling Team at London's Institute of Cancer Research, himself a computer scientist with a physics background (see From neutrinos to tumours). "But I would suggest definitely to take a course in statistics."

Computer scientists, on the other hand, need at least a basic understanding of biology. "It's essential, so they understand they're not just a bunch of numbers, that there's a person as the other end of these measurements," says Nick Luscombe, a computational biologist who studies gene expression at Cancer Research UK's London Research Institute and University College London. He also runs a smaller laboratory at the Okinawa Institute of Science and Technology in Japan. McDermott says that such people, sometimes come from physics and engineering backgrounds, are quite difficult to recruit. "These individuals don't always appreciate there's a lot of interesting research they can do in the cancer field."

There are also not many cancer fellowships and funding calls geared toward computing and mathematics. But the work of data scientists could also increase opportunities for biologists, he predicts, by democratizing the use of genomics. Biologists who aren't part of large cancer research centers will have access to these data sets and algorithms through cloud computing, and be able to make their own contributions to fighting cancer. McDermott says that some people believe future cancer research groups will be a 50-50 mix of data experts and wet lab scientists.

Another option is to do online courses like the Genetics and Genomcs Certificate offered by Stanford University. The course requires two core courses in the fundamentals of genetics and genomics, plus four elective courses on topics such as the genetics of cancer or the applications of gene therapy. It can be particularly useful for doctors treating cancer patients, says Michael Snyder, director of the Center for Genomics and Personalized Medicine at Stanford. "Many of these people got their MDs 15 years ago and the field didn't exist," he says.

Having a broader knowledge doesn't mean someone should aim to be an expert both in biology and computation, Luscombe says. "You run the risk of not being good enough at either," he warns. Kircher agrees: "in general you want to have one area where you are really, really strong and maybe one or two other areas that are really complementary to that," he says. One way to broaden expertise, he suggests, is to do more than one post-doctoral fellowship in different labs.

Physicists or mathematicians might be wary of moving into biology, which may seem absolutely alien to them. But the novelty of cancer genomics means they may be able to make bigger contribution than they could in more mature field, Kircher argues, and without a multi-year, multi-billion-dollar international effort. "There is so much stuff that has not yet been done," Sottoriva says. "You don't have to wait for another Large Hadron Collider to be built to answer questions in this field."

*This content was commissioned and edited by the Naturejobs editor*

## From neutrinos to tumours

ANDREA SOTTORIVA

Many cancer researchers started out as undergraduate biology students, but not Andrea Sottoriva. Now head of the Evolutionary Genomics and Modelling Team at London's Institute of Cancer Research, Sottoriva spent much of his time as an undergraduate and graduate student as a programmer for an experiment trying to detect neutrinos, elusive subatomic particles that can pass through the bulk of the Earth without slowing down.

But while he was working on his master's degree in computational modeling at the University of Amsterdam, which he finished in 2008, he started thinking about a different area of research. "There was this emerging field in bioinformatics and it caught my attention," he says. He was drawn by the opportunity to apply his research directly to health care, as well as by the recognition of how many open questions there were in this new field that computational modelling might address. He went on to earn a Ph.D. in cancer genomics and modelling from Cancer Research UK's Cambridge Research Institute, then did a post-doc at the Norris Comprehensive Cancer Center at University of Southern California, in Los Angeles, where he studied how genomic sequencing of multiple samples from a cancer patient could help in the understanding of how tumours evolve.

Cancer research is no longer solely the domain of biologists and medical doctors, thanks to the burgeoning field of genomics. "The cool thing is now in biology we have all this quantitative data, this digital data that we need computer technicians to analyze," Sottoriva says. "It is possible to really jump into this field which is becoming more and more interdisciplinary."

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## LIVER CANCER SCIENTIST

The Cancer Therapy and Research Center (CTRC) of the University of Texas Health Science Center at San Antonio invites applications from nationally recognized leaders in liver cancer research for a full time faculty position at the rank of Associate Professor/Professor (with tenure).

We seek an outstanding scientist with an active research program in liver cancer to lead a group of energetic and collegial basic, population, and clinician scientists with a diverse array of research interests including genetics, epigenetics, signal transduction, biomarkers, immunotherapy, novel therapeutic targets and modalities, and epidemiology related to liver cancer biology, etiology, and treatment. The successful applicant should hold an MD, PhD, MD/PhD, or equivalent degree and have a demonstrated track record of research productivity and successful extramural funding. Experience in obtaining multi-investigator research grants is desirable. Significant institutional support including a competitive compensation package, startup funds, and modern laboratory space and facilities will be provided. The successful candidate will also have opportunities to apply for additional support funds from a number of funding mechanisms administered by Cancer Prevention and Research Institute of Texas. The primary departmental affiliation of the faculty appointment will be in the Department of Microbiology and Immunology. A secondary appointment to another department may be considered based on the applicant's research interests and expertise.

The CTRC is one of three NCI-designated Cancer Centers in Texas and the only NCI-designated center in South Texas, serving a region of 45,970 square miles (or 4 million people) including a large, multiethnic population. The CTRC is committed to integrated multidisciplinary research and care, and the translation of research findings into the diagnosis, treatment, and prevention of cancer while improving the quality of life of cancer survivors. The 96 CTRC researchers have more than $61 million in extramural research funding and have a broad range of basic, clinical, and population science expertise. The CTRC's three research programs of Cancer Development and Progression, Experimental and Developmental Therapeutics, and Cancer Prevention and Population Sciences along with a group of developing programs are supported by eight shared core facilities. The University of Texas Health Science Center, San Antonio (UTHSCSA) (http://uthscsa.edu/) consists of five schools: School of Medicine (http://som.uthscsa.edu/), Graduate School of Biomedical Sciences (http://gsbs.uthscsa.edu/), School of Dentistry, School of Nursing and School of Health Professions. It is a highly integrated and translational research community, which includes the Cancer Therapy and Research Center (CTRC), a NCI-Designated Cancer Center, the Institute for Integration of Medicine and Science (IIMS) funded by a NIH Clinical and Translational Science Award (CTSA), the South Texas Research Facility (STRF), the Texas Biomedical Research Institute (TBRI), the Greehey Children Cancer Research Center Institute (GCCRI), the Barshop Institute for Longevity and Aging Studies, in addition to multiple hospitals, including the University Hospital and the Audie L. Murphy VA Hospital, and other clinical facilities.

San Antonio is the 7th largest city in the U.S. with a beautiful historical downtown area featuring the Riverwalk with its diverse entertainment and fine restaurants. UTHSCSA is located northwest of downtown San Antonio, gateway to the scenic Texas Hill Country, with many recreational options. San Antonio also has a low cost of living and an excellent public school system.

Applicants should send their inquiries and a copy of their NIH-formatted biosketch, a statement of research and teaching interests, recent publications and funding, along with three letters of recommendation to varnerl@uthscsa.edu, ATTN: Ian M. Thompson, MD, Director, Cancer Therapy and Research Center, 7979 Wurzbach Road, San Antonio, TX 78229.

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REGIONE TOSCANA is seeking outstanding candidates for the position of Scientific Director of ISTITUTO TOSCANO TUMORI (ITT), as the current incumbent will step down from this post in July 2015.

ITT is a Network Institute whose mission is TO UNDERSTAND, TO TREAT AND TO PREVENT CANCER AT BEST FOR ALL: therefore ITT seeks excellence in every aspect of Cancer research, Cancer care and Cancer prevention.

The Scientific Director will be appointed for 5 years and will be expected to provide leadership in all scientific, clinical and educational activities of ITT, jointly with the Operational Director.

Candidates must be internationally recognized in the area of Cancer Research/Oncology. Remuneration up to € 145,000.00 per annum.

Candidates wishing to manifest their interest are invited to send by 29th May 2015: (1) a statement declaring interest by completing a form downloadable from www.regione.toscana.it , (2) photocopy of identity card (3), CV, (4) list of most significant publications (max 20), (5) a letter explaining their motives. Applications must be addressed to *DG Diritti di Cittadinanza e Coesione Sociale, Settore Qualità dei Servizi, Governo Clinico e Partecipazione*, Via T. Alderotti 26/N, 50139 Firenze, Italy.

Full text of the advertisement is available on the site www.regione.toscana.it. Further particulars can be requested by emailing to segreteriaitt@regione.toscana.it.

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## Bioinformatician roles in the Manchester Centre for Cancer Biomarker Sciences

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The Cancer Research UK Manchester Institute, an Institute of the University of Manchester, is a world-leading centre for excellence in cancer research. The Institute is core funded by Cancer Research UK, the largest independent cancer research organisation in the world. We are adjacent to The Christie NHS Foundation Trust, one of the largest cancer treatment centres in Europe. We are establishing a Computational Biomarkers Team within the Manchester Centre for Cancer Biomarker Sciences and are seeking bioinformaticians with a strong desire to see their research and analyses translated directly to the clinic. The team will use DNA, RNA and protein based profiles derived from tumour biopsies, circulating tumour cells (CTCs) and/or ctDNA to derive robust patient classifiers. One specific goal of the biomarker centre is to develop blood tests that will use genomic / transcriptomic profiles to predict patient response to therapy and help personalise cancer patients' treatments.

### Computational Biomarkers Team Leader:

- Salary in the range of £28,000 - £45,700 dependent upon experience
- Job Ref: MI/15/23

We seek a highly motivated individual to lead this new team within the Manchester Centre for Cancer Biomarker Sciences. The successful applicant will have a background in statistical analysis of complex datasets and making inference in large-scale data using machine learning approaches, combined with a desire to see these approaches used for patient benefit. They will have a PhD in computational biology, mathematics, computer science or another related postgraduate degree, with extensive relevant experience along with previous experience managing a team, excellent communication skills and the ability to deliver a complex program of work to a deadline.

### Postdoctoral Scientist in Computational Biology:

- Salary in the range of £28,500 - £38,000 dependent on qualifications and experience
- Job Ref: MI/15/24

The successful applicant will join this team with a PhD in computational biology, mathematics, computer science or related discipline along with experience in applying machine learning techniques to large data sets and a familiarity with genomics and gene-expression data. They will be accomplished programmers with coding experience in R or MATLAB. Experience in writing parallel code and familiarity with best-practice approaches to software development, including unit testing and version control, would be advantageous.

Both roles are fixed term positions until 31 March 2017 (in the first instance). To apply for these positions please visit our website: www.cruk.manchester.ac.uk. The closing date for receipt of applications is: 15 May 2015.

**For any informal enquiries about these posts, please email Prof Caroline Dive or Dr Crispin Miller at caroline.dive@cruk.manchester.ac.uk or crispin.miller@cruk.manchester.ac.uk**

**For any queries regarding the application process contact the HR department on 0161 446 3231 or email jobs@cruk.manchester.ac.uk.**

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# Research Associates (Bioinformatics)

## Institute of Cancer and Genetics
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You will join an established team of bioinformaticians and laboratory staff within the Genomics Facility of Wales Gene Park, a NISCHR-funded facility based within the School of Medicine, Cardiff University. Established 2002, Wales Gene Park supports medical genetics and genomics research throughout Wales. Through our close collaboration with the All Wales Genetic Laboratory, our Genomics Facility deploys Illumina HiSeq, MiSeq, and Life Technologies Ion Torrent technologies to genomic data to support a diversity of clinically-orientated biomedical research in human cancers and medical genetics.

Alongside our existing team, and making use of our dedicated high performance computing infrastructure, you will provide bioinformatics support to handle, manipulate and analyse NGS data generated by the facility and external providers. You will provide specialist advice and experimental design expertise to colleagues looking to exploit exome-seq, RNA-seq, ChIP-seq, whole genome re-sequencing amongst other standard workflows as well as novel designs. You will also contribute to our various training programmes.

You will have a postgraduate degree in a relevant discipline and either have previous experience of bioinformatics or are newly qualified and wish to gain direct knowledge and experience of NGS technologies and analysis. You will be working closely with an established team of bioinformaticians so previous experience of handling Next Generation Sequencing data, whilst desirable, is not essential.

What is essential is that you have proven experience in writing software code in Perl, Python, Java, C/C++, or similar computer language, have good communication skills, are self motivated, and are willing and able to work accurately to a tight deadline. You will be expected to work within a Unix command line environment utilising standard pre-existing software packages and pipelines as well as your own bespoke software solutions. A background in biological sciences, whilst welcome, is not essential.

**Salary £31,342 - £37,394 per annum (Grade 6)**

**Informal enquires should be addressed to Dr Kevin Ashelford (AshelfordKE@cardiff.ac.uk).**

**Both positions are full-time (35 hours) and fixed-term until 31st March 2018.**

**Vacancy Number: 3212BR.**

**Closing date: Tuesday, 21 April 2015.**

**Please be aware that Cardiff University reserves the right to close this vacancy early should sufficient applications be received.**

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