



Laudatio for Dr. Elizabeth Murchison

Wellcome Trust Sanger Institute, Cambridge, UK

Winner of the Eppendorf Award for Young Investigators 2012

The laudatio was held by Prof. Reinhard Jahn (Director of the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany) at the prize ceremony in Heidelberg on May 9, 2012.

“It is common knowledge that cancer is the second leading cause of death among humans. Despite enormous investments in research the disease is far from being under control, and every one of us has a 20-25 % chance to die from the disease. We also know that cancer develops after somatic cells have accumulated mutations that eventually lead to malignancy – the uncontrolled division of cells that then result in tumors, often associated with the spreading of the cells through the organism. While there are important exceptions, most cancers are clonal, i.e. they are derived from individual precursor cells that frequently undergo further and often extensive mutagenesis during somatic proliferation. The only “positive” aspect about most cancers is that they are non-infectious – if a cancer cell is transmitted to another individual it is quickly recognized as foreign by the immune system of the recipient and dealt with accordingly. The only exceptions from this rule are cancers caused by oncogenic viruses that are infectious agents and that may lead to the generation of tumors in the recipient.

However, evidence is accumulating that there may be a second, and in a way scarier route for tumors to spread between individuals: the direct transmission of tumor cells. One example includes an infectious genital tumor affecting dogs, termed canine transmissible venereal tumor. This tumor that is transmitted during sexual intercourse is known since more than 100 years, and it

affects dogs around the world. Recent genetic analyses of tumor samples from distant regions allowed for the conclusion that the tumor is very likely to be clonal and may have originated from a dog or wolf many centuries ago, probably making this the oldest and most propagated mammalian cell line.

There is a second example of a clonal cancer transmitted between an individual that in recent years has captured the attention of the news media, and this where our Eppendorf Award winner, Elizabeth P. Murchison, has made seminal contributions. It affects the Tasmanian devil, the largest surviving marsupial carnivore that is endemic to the island of Tasmania. The Tasmanian devil is acutely threatened with extinction due to the spread of a particularly ugly cancer, termed Tasmanian devil facial tumor disease. This tumor was first noticed in the year 1996 and is now spreading fast through the entire population. The cancer is transmitted from animal to animal during social interactions and fights (apparently they are rather belligerent, at least occasionally), and this is why the tumors usually develop in the head region. Once the cancer begins to develop, the animals die within 6-9 month, while the normal life expectancy is more than 5 years.

Elizabeth Murchison grew up in Tasmania, and since she loves the outdoors she is very familiar with the Tasmanian devil since young age. Being fascinated by the human genome project during her high school years she decided to pursue a career in molecular biology. After graduating from the University of Melbourne she joined the lab of Greg Hannon at the Cold Spring Harbor Laboratory for her PhD. Greg is an international leader in the field of small RNAs. Elizabeth did very well in Greg's laboratory, with several first author publications in leading journals to her credit. After receiving her Ph.D. in the year 2007 she remained for another year in the Hannon lab before moving to the Wellcome Trust Sanger Institute where she has been since.

Elizabeth's fascination with the Tasmanian devil tumor facial tumor disease dates back to the year 2005. Back home in Tasmania for a visit she found a dead Tasmanian devil on the roadside with a small tumor. Intrigued by this incident she actually obtained a sample from the tumor and decided – despite her growing focus in the field of small RNAs – to devote her training as molecular biologist to the study of this threatening disease. During that time, the spread of the disease was mainly attributed to a virus although the idea that the disease may also spread by direct transfer of cells (allograft theory) was already articulated. Shortly thereafter, additional support for the clonal origin was derived from a small study in which tumor samples from several individuals were karyotyped.

Elizabeth then used her training in molecular biology to tackle the problem of the cancer “head-on”. First, she used large-scale genetic approaches such as the analysis of microsatellite DNA and mitochondrial DNA (both of which vary between individuals) to show that the tumors of different individual devils are indeed all originating from the same parent tumor, thus unequivocally proving that this cancer is spreading by direct transfer of cells. Deep sequencing of the transcriptome then revealed that the tumor is probably of Schwann cell origin, i.e. derived from cells whose normal business is to electrically insulate peripheral nerve cells. Elizabeth then used the support of the Sanger institute, encouraged and supported by her mentor Mike Stratton, to completely sequence the genome of two individuals of the Tasmanian devil and of two independently obtained tumor samples, complemented by an analysis of genetic diversity of more than 100 different tumor samples collected during the past years. The result of this work, published in two major articles in top journals, represents not only a milestone in the field but also opens fascinating new questions such as how these transmissible cancers evade the immune system of multiple individuals. The work may also turn out to be more important to human health than originally anticipated. Indeed, there are indications that direct transmission of tumors by cell transfer may also (albeit rarely) occur in humans.

The work of Elizabeth Murchison stands out as exemplary, and it shows how the commitment of a single person who is well trained and uses her training to address a biological problem can have a major impact. It also shows that research in a seemingly esoteric field (a strange tumor in an exotic species) can yield fundamental scientific insights and open new avenues for research relevant for human health.”