A Pioneer in Tumor Virology

Marguerite Vogt (1913-2007), a groundbreaking cancer researcher and virologist, was one of the outstanding scientists of the 20th century. Born in Berlin as the youngest daughter of Oskar Vogt and Cécile Vogt-Mugnier, she would have celebrated her one hundredth birthday this year. She studied medicine at Friedrich Wilhelm University in Berlin and was a doctoral student of Nikolaj V. Timoféef-Ressovsky in Berlin-Buch. A scientific symposium will take place in her honor at the MDC on December 10, 2013. Here is an abbreviated version of an essay about Marguerite Vogt by Professor Wunderlich.

Marguerite Vogt continued actively working as a laboratory researcher until the year 2000. Picture: Photo Courtesy of the Salk Institute for Biological Sciences

Volker Wunderlich (born in 1939) obtained a degree in Chemistry from the University of Leipzig in 1962 with a thesis on physical chemistry. He went on to pursue doctoral studies in Biochemistry (with a focus on mitochondrial DNA), receiving the title Dr. rer. nat. in 1969 from University of Halle, and received in 1982 an academic appointment in Brlin on the topic of retroviruses. He studied under Prof. Arnold Graffi. In 1985 he was appointed Professor of Biochemistry. In Berlin-Buch he held positions at the Cancer Research Institute of the Academy of Sciences (1964-1991), where he was department head from 1976-1991, and the MDC (1992-2004). He has held teaching positions in Halle, Leipzig and Berlin (at Humboldt-Universität). In 1995 he had a guest professorship in Essen. He specialized in the areas of experimental cancer research with an emphasis on chemical carcinogens, tumor virology and the molecular biology of tumors. Since his retirement in 2004, Prof. Wunderlich has published widely on topics in the history of science. Photo: David Ausserhofer

Growing up as a child of famous parents is a privilege and an inspiration, but at the same time can also be a burden for those affected. As far as is known, Marguerite Vogt, who was born in Berlin on February 19, 1913 as the younger daughter of the brain researchers Cécile and Oskar Vogt, did not have any problems with this situation. She already knew at a young age that she wanted to become a scientist, just like her sister Marthe, who was ten years older and who became a renowned neuropharmacologist. Marguerite studied medicine at Friedrich Wilhelm University in Berlin and graduated in September 1936. She then worked under the supervision of Nikolaj V. Timoféeff-Ressovsky in Berlin-Buch in the Genetics Department of the Kaiser Wilhelm Institute for Brain Research on her dissertation, which she defended one year later. Her dissertation in the field of medicine included experimental studies on the fruit fly Drosophila melanogaster and explored questions of penetrance, expressivity and the specificity of mutated genes. This area of research was initiated by Oskar Vogt and Timoféeff. Until the outbreak of the Second World War, Marguerite Vogt then worked in Paris as a postdoctoral fellow under the guidance of the geneticist Boris Ephrussi.

From1939 until 1950 she conducted genetic studies on the hormonal influence of developmental processes on Drosophila at her father's institute in Neustadt (Black Forest) and published these in 38 original papers, including one in the journal Nature in 1946 (!). The results of these studies are now regarded as ahead of their time.
In June 1950, through the mediation of Hermann J. Muller and Max Delbrück, Vogt obtained a new postdoctoral position at the California Institute of Technology (Caltech) in Pasadena (USA) where she initially worked with Delbrück in the field of bacterial genetics. Then, at Delbrück's suggestion, in the summer of 1952 she began a long-standing, very successful collaboration with the Italian-born molecular biologist Renato Dulbecco (1914 - 2012). This collaboration continued from 1963 to 1972 at the Salk Institute for Biological Studies in La Jolla, California.
In 1954 the two scientists developed the first plaque assays in tissue culture (plaques are areas of dead cells in an otherwise healthy cell monolayer) for animal virus strains – i.e. for the poliomyelitis virus and the Western equine encephalomyelitis virus. These plaque assays were used to determine the number of plaque-forming units in a virus sample in order to estimate the number of single virus particles, to analyze the virus growth cycle and to isolate genetically pure virus strains and mutants. Through this research the two scientists founded the field of molecular virology. Since the safety precautions we take for granted today did not exist or were not practiced at that time, working with living pathogenic viruses was not at all without risk. The results found immediate practical application in the production of the Salk polio vaccine. Later on, similar plaque assays were developed for numerous cytopathogenic viruses isolated and characterized by other scientists. Of particular significance was the development of the first cell culture focus-forming assay for the tumorigenic Rous sarcoma virus, which Howard Temin and Harry Rubin carried out in the lab of Dulbecco and Vogt. Thus, for the first time a quantitative test was available for the neoplastic transformation of *in vitro* cultivated cells, an early milestone in the history of molecular tumor biology. From 1959 on, Vogt and Dulbecco conducted their own research on tumor viruses. Shortly before that, the tumorigenic polyoma virus had been discovered, which at that time was still largely unknown. Dulbecco and Vogt identified it as a DNA virus with a small ring-shaped genome. They showed that the virus is able to transform embryonic cells in tissue culture into malignant growth. Virus production could be induced in mouse cells, which led to the demise of the cells. Hamster cells, however, were transformed; they usually did not produce any virus, but were resistant to a super infection. All attempts to induce virus production in these cells were unsuccessful. A short time later, Dulbecco and his team of researchers were able to show for the first time that the virus DNA can be stably integrated into the cell genome as a provirus. As a result of these studies it was found that normal cells can be transformed into cancer cells outside of the organism and that tumor viruses contain genes that are responsible for this. After Dulbecco left the Salk Institute for a period of time, the collaboration with Vogt ended. In 1973 Marguerite Vogt was appointed Research Professor (later Professor of Molecular and Cell Biology) at the Salk Institute and from then on focused on recombinant RNA tumor viruses. She published papers on the synergism of viral oncogenes and on the autocrine growth of T-cell lymphomas, among other topics. Even at an advanced age she worked every day in the laboratory. She was already over 85 years old when she published her last paper on replicative senescence of human fibroblasts.

Although Marguerite Vogt never received a major award, she had an exceptionally high reputation within the scientific community. Her enthusiasm for science was legendary. She was not bothered by the fact that Dulbecco received many awards for their joint work (among these the Nobel Prize in 1975), because she placed little value on such honors. She was an influential mentor and colleague of several future Nobel laureates. "She's certainly one of the best and most intelligent scientists I know," Edward Lewis, one of the Nobel prizewinners, said later. Outside the lab she impressed listeners with her excellent piano playing, often together with Dulbecco, who was also very musical. She loved literature, which she could read in the original in six languages. In 2001 the Marguerite Vogt Endowed Lecture was established at the Salk Institute – a very fitting tribute to this remarkable woman. Marguerite Vogt died in La Jolla, California on July 6, 2007.

More information about the symposium can be found at: https://www.mdc-berlin.info/events/691238/12010

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