Studies in History and Philosophy of Biological and Biomedical Sciences 48 (2014) 185–188

Contents lists available at ScienceDirect

Studies in History and Philosophy of Biological and Biomedical Sciences

journal homepage: www.elsevier.com/locate/shpsc

Introduction

Following cancer viruses through the laboratory, clinic, and society

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ARTICLE INFO

Article history:
Available online 16 October 2014

ABSTRACT

These essays in this special issue follow cancer viruses as a means of better understanding the history of biomedicine. Spanning the worlds of chronic and infectious disease research, the history of cancer viruses touches upon an enormous diversity of settings and scientific disciplines. Cancer viruses appeared during the twentieth century as vaccine targets, vaccine contaminants, laboratory anomalies, and tools for molecular biology. Rather than picking one discipline or setting to privilege above others, this issue suggests what can be learned, not only about cancer viruses but also about the character of modern biomedicine, from following these viruses through their different historical trajectories.

There is a long history to the fear that cancer might be contagious. At the end of the 19th century, however, this fear was tempered by the new hope that discovering a cancer-causing infectious agent would enable the large scale prevention of cancer. This hope centered on the identification of cancer viruses. The six essays gathered in this issue provide a synoptic account of the pathways of cancer virus research and the research trajectories of cancer viruses ever since. These attempts to understand the relationship between viruses and cancer occupy a middle ground in the well-known transition from infectious to chronic diseases as the main focus of public health in industrial societies. Befitting this intermediate status, inquiries into the nature of cancer viruses incorporated practices from epidemiology, immunology, microbiology, virology, pathology, genetics, and molecular biology. By following viruses themselves from place to place and discipline to discipline, these essays individually and collectively shine new light on the critical roles that cancer viruses have played in the production of knowledge in a wide range of biomedical fields. Starting at the beginning of the twentieth century, Neeraja Sankaran contrasts the biography of Rous Sarcoma Virus with bacteriophage, and shows the importance of analogies between the two for the development of virology and early molecular biology. Moving forward, Gregory Morgan examines the discovery of mouse leukemia viruses, a crucial event in the revival of cancer virus research in the middle of the twentieth century. Next, Brendan Clarke uses the history of Epstein Barr Virus to pose new questions about space and scale in cancer research; Laura Stark and Nancy Campbell follow the unexpected appearance of Simian Virus 40 as a possible oncogenic virus in human research settings; and Robin Scheffler raises the possibility that our understanding of the history of cancer viruses should also include viruses which are now thought not to exist, in this case a childhood leukemia virus. Finally, looking at the present, Alex Broadbent considers how the relationship between Human Papilloma Virus and cervical cancer forces us to clarify our understanding of what it means for a virus to "cause" cancer and the consequences this has for classifying illness.

While cancer viruses have not lacked for chroniclers, the sinuous path of cancer viruses through the twentieth century fits uneasily into the history of cancer, medicine, or biology. The historiography of cancer tends to emphasize clinical treatment,

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http://dx.doi.org/10.1016/j.shpsc.2014.09.004
1369-8486/

authority, and culpability, arenas where cancer viruses do not usually appear.[1] Likewise, cancer viruses have fallen into the divide between the clinic and the laboratory in the historiography of biology and medicine. Following the "social turn" historians of medicine sought to deemphasize the laboratory in their narratives while historians of biology focused on the creation of laboratory-based experimental systems far removed from the concerns of the clinic. Neither of these agendas captured the full set of activities associated with cancer viruses. Fortunately these divisions are eroding, and interest in the overlap of biology and medicine—biomedicine—is on the rise (Huisman & Warner, 2004; Keating & Cambrosio, 2004; Löwy, 1996, 2011).

As "tracers" for uniting the different sites and practices involved in writing a richer history of biomedicine, cancer viruses are exceptional precisely because of their multifaceted and unresolved history.[2] Until the late twentieth century, the idea that cancer might be caused by an infectious agent offered the most therapeutically-relevant path of inquiry into the etiology of cancer. Demonstrating the genetic origins of cancer presented no hope for prevention or therapy, while exposure to environmental or chemical carcinogens could at best be ameliorated when such compounds were identified. By contrast, the identification of an infectious agent responsible for cancer promised widespread prevention through vaccination. Yet this promise did not immediately translate to enthusiasm for cancer virus research. The separation of infection from other environmental or hereditary causes of disease was rarely so clear as advocates of bacteriology made it out to be (Löwy & Gaudillière, 2001). Even for bacteriologists, the techniques which worked well to reveal bacteria were incapable of visualizing viruses. For example, in 1911 the pathologist Peyton Rous determined that that agents smaller than bacteria were capable of transmitting tumors from one chicken to another. At an early point, Rous was tempted to identify this agent as a virus. However, he was unable to isolate it, and without a definite agent his laboratory findings seemed to fly in the face of clinical experience: doctors and nurses working in cancer wards did not catch cancer (Becsei-Kilborn, 2010; Helvoort, 2004).

After several decades of muted activity, interest in cancer viruses began to revive in the 1940s with the discovery of mammalian papilloma viruses and the development of instruments, such as the electron microscope or ultracentrifuge, which allowed the treatment of viruses as physiochemical objects in the laboratory (Creager & Gaudillière, 2001; Kevles, 1995). As Morgan describes, this revival received further impetus from Ludwik Gross's discovery of cancer causing viruses in mice during the 1950s, animals whose relevance to human disease was more widely accepted than chickens. The release of the polio vaccine inspired considerable optimism for vaccination as a public health measure, and during the 1960s, cancer viruses were the focus of an intense research campaign at the United States National Cancer Institute. Meanwhile, molecular biologists such as Renato Dulbecco developed tissue culture methods for the reproduction of animal viruses *in vitro* which were used to study a growing number of animal tumor viruses (Kevles, 1993). In the 1970s, cancer virus research resulted in the identification of cancer causing genes, or oncogenes, in both viruses and normal animal cells (Fujimura, 1996). Before the widespread adoption of PCR and restriction enzymes, cancer viruses provided one of the few means of manipulating individual genes in eukaryotic cells (Müller-Wille & Rheinberger, 2012, p. 162). In the 1980s and 1990s viruses were eclipsed by interest in the genetic basis of cancer. With work on the human genome, the discovery of oncogenes appeared to provide an ironic coda for cancer virus research—the search for an external cause of cancer had revealed a quintessentially internal cause (Helvoort, 1999; Klein, 1999; Weinberg, 1998). Recently, the development of the Human Papilloma Virus vaccine as a preventative for cervical, oral, and anal cancers promises to fulfill earlier hopes of vaccination, although not without controversy (Wailoo, Livingston, Epstein, & Aronowitz, 2010).

Following cancer viruses grants insight into how biomedical research understands (or fails to understand) its objects of inquiry. While the history of science and medicine tends to focus on moments of understanding, the productivity of cancer viruses in biomedicine often emerged from their ambiguity. Sankaran's parallel biographies of bacteriophage and Rous Sarcoma Virus illustrate this point neatly. The occurrence of cancer by viral infection seemed counterintuitive for the reason that viral infection typically killed cells. Unlike these infections, cancer viruses had the ability to "transform" cells, causing abnormal growth that appeared to be experimental precursor to cancer. She describes how the analogy drawn between transformation and bacterial lysogeny (the non-fatal infection of *E. coli* bacteria by bacteriophage virus) in the 1950s allowed the convergence of geneticists, bacteriologists, and virologists on cancer viruses, a mixing of scientific styles which helped shape the approach of molecular biology to eukaryotic animal cells. The very traits which made cancer viruses anomalous allowed a new understanding of viruses. Broadbent shows how the unique features of cancer viruses, especially the long period of asymptomatic latency between infection and the occurrence of cancer, provide an opportunity to reexamine the meaning of health—is it equivalent to the absence of disease? Broadbent considers the case of Human Papilloma Virus and cervical cancer, particularly the complex chain of events between infection and tumorgenesis, to refine our understanding of why medicine should (or should not) classify diseases as a function of their causes.

Efforts to resolve the ambiguity of cancer viruses have made explicit the considerable social and experimental work that goes into the constitution of "biomedical objects."(Daston, 2000) Stark and Campbell draw attention to the importance, for both biomedical research and historical narrative, of the unexpected. They present the case of Simian Virus 40, a "stowaway" in the process of polio vaccine production. Initially a vaccine contaminant, the encounter of Simian Virus 40 with cancer virus researchers at the National Cancer Institute raised the frightening possibility that millions had been exposed to a cancer-causing virus. More than a threat to the safety of the polio vaccine, the unexpected appearance of Simian Virus 40 was a productive event. Critically, the appearance of stowaways carried important ethical and political stakes for biomedical research. In this instance, the appearance of Simian Virus 40 in a study of respiratory illness allowed researchers to convert this trial into one of the few that tested the carcinogenic potential of a virus directly in human subjects.

Stark and Campbell raise the question of what ontological status objects like cancer viruses should possess in narratives of biomedicine. Should retrospective knowledge of current science

[1] Writing a generation ago, David Cantor observed that the historiography of cancer was sharply split between social and experimental accounts.(Cantor, 1993) This has changed dramatically in the last decade. The most prominent concentrations of scholarship include those on the link between smoking and lung cancer(Brandt, 2007; Proctor, 2011), the contest between doctors and patients for authority over cancer, especially breast cancer, treatment (Aronowitz, 2007; Cantor, 2006a, 2006b; Gardner, 2006; Leopold, 1999; Lerner, 2001), breast cancer genetics(Cantor, 2006a, 2006b; Necochea, 2007; Palladino, 2002; Parthasarathy, 2007), and the hazards of environmental carcinogens(Brown et al., 2006; Langston, 2010; Proctor, 1995). Particularly relevant for historians of biomedicine and cancer viruses are a set of studies focusing on how knowledge of cancer is produced not only through laboratory studies but through practices such as clinical trials and diagnosis. (Keating & Cambrosio, 2012; Löwy, 2010; Timmermann, 2013).

[2] This notion of a historical "tracer" is drawn from Angela Creager's recent study of radioisotopes. (Creager, 2013).