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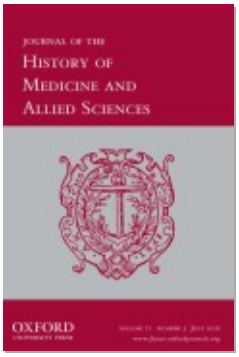

Journal of the History of Medicine and Allied Sciences, Volume 71, Number 3, July 2016, pp. 271-292 (Article)

Published by Oxford University Press

Journal of the History of Medicine and Allied Sciences, Vol. 71, No. 3, pp. 271–292
doi: 10.1093/jhmas/jrv057
Advance Access Publication: January 18, 2016

OXFORD

The Microscope against Cell Theory: Cancer Research in Nineteenth-Century Parisian Anatomical Pathology

LAURENT LOISON

Cavaillès Center for the History and Philosophy of Science, USR 3608, ENS, Paris, France. Email: laurentloison@yahoo.fr

ABSTRACT

This paper examines the reception of cell theory in the field of French anatomical pathology. This reception is studied under the lens of the concept of the cancer cell, which was developed in Paris in the 1840s. In the medical field, cell theory was quickly accessible, understood, and discussed. In the wake of research by Hermann Lebert, the cancer cell concept was supported by a wealth of high-quality microscopic observations. The concept was constructed *in opposition* to cell theory, which appears retrospectively paradoxical and surprising. Indeed, the biological atomism inherent in cell theory, according to which the cell is the elementary unit of all organs of living bodies, appeared at the time incompatible with the possible existence of pathological cells without equivalent in healthy tissues. Thus, the postulate of atomism was used as an argument by Parisian clinicians who denied the value of the cancer cell. This study shows that at least in the field of anatomical pathology, cell theory did not directly result from the use of the microscope but was actually hindered by it.

KEYWORDS: cell theory, cancer cell, anatomical pathology, nineteenth-century Parisian medicine, Hermann Lebert

The creation of an autonomous science of living organisms in the nineteenth century relied on two fundamental biological theories, cell theory and Darwinian evolutionism.[1] Yet, so far, these two theories have received unequal attention from historians of science. While the reception of Darwinism in different disciplinary contexts and varied national and local traditions has, for example, been addressed in numerous

1 Daniel J. Nicholson, "Biological Atomism and Cell Theory," *Stud. Hist. Philos. Biol. Biomed. Sci.*, 2010, *41*, 202–11, 202.

extensive studies,[2] nothing comparable has been published on cell theory.[3] The objective of this paper is therefore to help fill this historiographical gap.

Here, the reception of cell theory in the French anatomical pathology and clinical fields will be investigated using the debates in mid-nineteenth-century Paris over the nature and diagnosis of cancer. In the early 1840s, Parisian microscopists argued that there was a cell type specific to cancer, and that microscopic analysis could ensure reliable diagnosis. This was the beginning of a long opposition between clinicians and microscopists. The general context of this dispute has been studied in great detail by Ann La Berge, who published three richly documented papers on the subject. She showed first the progressive introduction of the microscope into Parisian medical research at the turn of the 1840s, in particular through the teaching of foreign physicians.[4] She subsequently investigated the complex relationships between the dominant clinical tradition and the new micrographic school in the 1840s and 1850s. Her main conclusion was that unlike what Erwin Ackerknecht had argued,[5] the clinicians had not dismissed the microscope entirely; their response was more nuanced: "although the Paris school did not embrace microscopy, neither did its leader reject it."[6] Lastly, La Berge used the famous debate held in 1854–55 at the Academy of Medicine regarding the use of the microscope in pathological anatomy to highlight "the role of debate as scientific practice" in the nineteenth century, which she argued reflected "a shared masculine culture of honor."[7]

Having systematically examined the same corpus, I concur with most of the theses defended by La Berge. The intention of this paper is neither to refute them (with one exception, in the fourth section) nor to complement them; based on the same historiographical material, I propose *another reading* of that history. The paper will focus specifically on cell theory and its reception in Parisian medicine. The elaboration of the "cancer cell" concept in Paris during the 1840s and 1850s offers an excellent vantage point from which to study this reception and the relations between the nascent theory and the empirical data available at the time.

2 See, for example, Eve-Marie Engels and Thomas F. Glick, *The Reception of Charles Darwin in Europe* (New York: Bloomsbury Publishing, 2009); for the French case, see Yvette Conry, *La réception du darwinisme en France au XIX^e siècle* (Paris: Vrin, 1974).

3 On the reception of cell theory in Britain, see L. S. Jacyna, "The Romantic Programme and the Reception of Cell Theory in Britain," *J. Hist. Biol.*, 1984, *17/1*, 12–48; in Italy, see Ariane Dröscher, "La 'Cellularpathologie' di Rudolf Virchow e il rinnovamento della medicina italiana nella seconda metà dell'Ottocento," *Ann. Ist. Stor. Italo-ger. Trento*, 1998, *24*, 87–113; in France, see Laurent Loison, "Pourquoi refuser la théorie cellulaire? Le projet d'une anatomie chimique chez Charles Robin (1821–1885)," *Rev. Hist. Sci.*, 2015, *68/1*, 23–45.

4 Ann La Berge, "Medical Microscopy in Paris, 1830–1855," in *French Medical Culture in the Nineteenth Century*, ed. Ann La Berge and Mordechai Feingold (Amsterdam, Atlanta: Rodopi, 1994), 296–326.

5 Erwin Ackerknecht, *Medicine at the Paris Hospital, 1794–1848* (Baltimore: Johns Hopkins Press, 1967), 121–27.

6 Ann La Berge, "Dichotomy or Integration? Medical Microscopy and the Paris Clinical Tradition," in *Constructing Paris Medicine*, ed. Caroline Hannaway and Ann La Berge (Amsterdam, Atlanta: Rodopi, 1998), 275–312, 276.

7 Ann La Berge, "Debate as Scientific Practice in Nineteenth-Century Paris: The Controversy over the Microscope," *Perspect. Sci.*, 2004, *12/4*, 424–53, 425.

In order to have a clear grasp of the epistemological implications of this reception, it is necessary to start with a sound understanding of the contents of cell theory. The standard cell theory developed by Robert Remak and later Rudolf Virchow is traditionally presented as based on two claims: first, the principle of genetic continuity among all cells (*omnis cellula e cellula*) and second, a postulate of atomism specifying that the cell is the basic element of all living organisms and is the smallest living entity.[8] In the context of cell theory, biological atomism[9] does not mean that cells were seen as simple particles, like atoms in physics. It consisted in the view that cells, as irreducible elements of all living organisms, were themselves alive and had a dominant role in the functioning of living beings.

These two core components, however, have had neither the same scope nor the same place within cell theory: biological atomism is consubstantial to this theory, and was only later joined to the principle of genetic continuity, with the rejection of the earlier dominant theory of "blastemic formation" in which cells arose by spontaneous generation in bodily fluids. So the blastemic theories of Schleiden and Schwann on the one hand, and those of Remak and Virchow on the other, were both identified as forms of cell theory, although they differed radically as to their proposed mechanisms of cell production. Even though it appears that in Schwann's work, the process of cytoblastemic genesis may have been of greater importance than the postulate of atomism,[10] the fact remains that the latter had sustained wide support since 1839.[11] For the case at hand, the distinction between the mechanism of cell formation and the idea that the cell is the basic unit of living organisms is critically important, since, as we will see, these two components of cell theory were received very differently.

Another crucial distinction is that between cell theory proper and the more general—and far less contested—idea that cells are parts of living things. Very quickly at the beginning of the nineteenth century, the cellularity of at least some structures that constitute organisms was acknowledged by most if not all naturalists and physiologists. For instance, the cellularity of plants was widely taken for granted well before the birth of cell theory. This process of the "cellularization" of the fields of anatomy and physiology did not imply the acceptance of cell theory. This is precisely what happened in Paris regarding the issue of cancer: Parisians microscopists were carefully describing and characterizing cancer cells while, at the same time, making clear their firm opposition to cell theory and, especially, biological atomism.

The second difficulty specific to this history is that it unfolded within the context of a growing rivalry between France and the German-speaking regions. There was

8 Henry Harris, *The Birth of the Cell* (New Haven and London: Yale University Press, 1999); Nicholson, "Biological Atomism and Cell Theory."

9 The term "atomism" was not used by physicians at the time of the birth of cell theory. Following several contemporary historians and philosophers (for instance, Nicholson), I use it in this paper because it concisely encapsulates a complex set of ideas.

10 See Ohad Parnes, "The Envisioning of Cell," *Sci. Context*, 2000, *13/1*, 71–92, 83–85; and Ohad Parnes, "From Agents to Cells: Theodor Schwann's Research Notes of the Years 1835–1838," in *Reworking the Bench, Research Notebooks in the History of Science*, ed. Frederic L. Holmes, Jürgen Renn, and Hans-Jörg Rheinberger (Dordrecht, Boston, London: Kluwer Academic Publishers, 2003), 119–39, see esp. 131.

11 François Duchesneau, *La genèse de la théorie cellulaire* (Montréal, Paris: Bellarmin, Vrin, 1987), 71.

undeniably a nationalist component to some of the debates and oppositions. Nevertheless, it seems possible to neutralize this complication to a great extent by making explicit what the Parisian side meant by "German." The main reproach formulated against German ideas for much of the nineteenth century, during the heyday of positivism, was that they were mostly speculative, i.e., outrageously theoretical. This was one of the objections lodged against the atomism of cell theory. The point here is not to take sides between the opposed interpretations by Timothy Lenoir and Robert Richards regarding the metaphysics involved in the rise of cell theory in Germany.[12] Regardless of whether cell theory owed its origins to a "teleomechanistic" agenda or to *Naturphilosophie*, it was met with skepticism in Paris. It is important to note that German research was not rejected wholesale on the grounds of the nationality of its authors. The leader of the Parisian school, Hermann Lebert, was himself Prussian, suggesting that the term "German" was often used for rhetorical purposes during the numerous debates that punctuated this history.

For some thirty years, a number of historians of science have seriously called into question the idea that cell theory was mainly the consequence of the introduction of the new achromatic microscopes developed in the 1820s.[13] Ohad Parnes, in particular, based on an in-depth study of Theodor Schwann's laboratory notes, was able to retrace the path that led the German physiologist to the first genuine formulation of a cell theory of biological organization. Parnes has no doubt that although the microscope was clearly an indispensable tool for Schwann, it was never the starting point or the basis of his theoretical work.[14]

The present study supports a similar nonempiricist take on the history of cell theory. It defends the thesis that in the case of the pathological anatomy of cancer, cell theory was disputed *because of the use of the microscope*. Indeed, it shows that the "cancer cell" concept, undoubtedly derived from the first phase of the "cellularization" of the nascent field of biology, was conceived in Paris as an unassailable empirical finding that would make a serious dent in the extension of cell theory. More precisely, for the actors involved at the time, there was a radical incompatibility between the biological atomism inherent in that theory and the possibility that authentically cancerous cells could exist within organisms. The cancer cell, as a medical tool for improving the quality of the diagnosis of malignant tumors, had to be morphologically specific, displaying distinctive features—such as a very large nucleus—that were not found in healthy tissues. Cell theory, however, implied a vision of biological organisms that was not compatible with such forms of radical specificity: as each part of an organism was necessarily composed of cells, diseases that developed in it were solely cell dysfunctions. In other words, diseases had no ontology of their own, and cancer was no exception to the rule. As a result, for advocates of cell theory like Virchow, the

12 Timothy Lenoir, *The Strategy of Life, Teleology and Mechanics in Nineteenth-Century German Biology* (Chicago and London: The University of Chicago Press, 1989); Robert J. Richards, *The Romantic Conception of Life, Science and Philosophy in the Age of Goethe* (Chicago and London: The University of Chicago Press, 2002).

13 Duchesneau, *La genèse de la théorie cellulaire*, 12.

14 Parnes, "The Envisioning of Cell," 88; Parnes, "From Agents to Cells," 134.

growth of a cancerous tumor could not be traced to the genesis of specific cells, and instead consisted in the partial transformation of cells in the damaged tissue. This is why—in a surprising and opportunistic manner—Parisian clinicians in the wake of the powerful Alfred Velpeau lent their support to cell theory against Parisian microscopists, arguing that it defeated the concept of cancer cell and accordingly confirmed the primacy of clinical medicine over microscopy.

The first section of this paper provides a brief analysis of the channels through which German-language cell theory was introduced to the Parisian medical community in the 1840s. It happened quickly and on a large scale, with the contents of the main texts made quickly accessible to French physicians, a great majority of whom did not read German. The second section examines the painstaking account of the genesis of the concept of the cancer cell in the work of the pathologist Hermann Lebert. Lebert detailed the morphological criteria that distinguished authentically cancerous cells on the basis of innumerable microscopic observations conducted for over ten years in Parisian hospitals. He reported his findings in three massive volumes, published in French between 1845 and 1861, which were at the time unequaled in European scholarship. The third section offers a new interpretation of the successive debates that took place in Paris on the diagnosis of cancer (1844–55), approaching them as a dispute between proponents and opponents of cell theory. Under the influence of Velpeau, the clinical physicians, who wished to retain their prerogatives, embraced Schwann and Müller's theses. At the same time, the micrographic school of Paris rallied around Lebert in opposing the atomism of cell theory. Lastly, the fourth section explores the outcome of these debates. It shows that beginning in the late 1850s, as cell theory gained recognition in Paris, support for the concept of the cancer cell gradually eroded, finally to such an extent that the very status of cancer as a distinctive disease came to be denied.

THE INTRODUCTION OF CELL THEORY IN PARISIAN ANATOMICAL PATHOLOGY: AN OVERVIEW

The history of the progressive and difficult introduction of microscopy into the field of Parisian medicine has already been very well documented by La Berge; readers eager to learn more will find her 1994 paper rewarding.[15] According to her, we can clearly identify four microscopists who played a key role in the lasting introduction of this practice in Parisian medicine during the 1830s and 1840s: Alfred Donné, David Gruby, Louis Mandl, and Hermann Lebert.[16] Alfred Donné was the only Frenchman among the four. Gruby and Mandl were Hungarian, and Lebert was Prussian. The latter three moved to Paris around 1840, a period during which Schwann published his findings on cell theory, when Parisian medicine still enjoyed a dominant status in Europe.[17] Only Mandl and, of course, Lebert appear to have played important roles in the introduction of this theory to the Parisian medical school, which will be recounted in

15 La Berge, "Medical Microscopy in Paris."

16 Ibid., 298–99.

17 Theodor Schwann, *Mikroskopische Untersuchungen über die Uebereinstimmung in der Struktur und dem Wachstum der Thiere und Pflanzen* (Berlin: Sander'schen Buchhandlung, 1839).

broad strokes here. This section will examine the convergence in Paris during the first half of the 1840s of two crucial questions: first, about the nature of cancer, which had already been debated for several decades,[18] and second, about the cellularity of animal tissues.

Until the second half of the 1830s, cancer was studied almost exclusively in its clinical dimensions. The growth of tumors was observed at the patient's bedside. If cancerous, such growths would recur even after surgical removal. From a clinical standpoint, defining and diagnosing cancer with certainty was extremely complex: most physicians did not see essential differences between inflammation, cancer, and ulcer; and they found it particularly difficult to distinguish the various forms of tumors from healthy surrounding tissues.[19] For many clinicians, cancer was a "homomorphous" (or homologous) disease: cancer tissues were homologous with healthy tissues found elsewhere in the body (or at an earlier stage of ontogeny). Inspired by René Laennec, some, however, saw cancer as a clearly distinguishable, "heteromorphous" (or heterologous) disease because it consisted of tissues that had no equivalent elsewhere in the body. This distinction would become an important bone of contention in the controversies over cancer diagnosis.

During the 1830s, numerous, almost simultaneous attempts were made to identify chemical and morphological markers of cancer. Following the hypothesis that cancer was a specific disease with its own ontology, it made sense to try to identify chemical components and/or microscopic morphological features characterizing it. The chemical efforts quickly turned out to be a dead end;[20] the only hope that remained was the possibility of observing structures specific to cancer under the microscope.

Leland Rather and Ann La Berge both contend that the first microscopist to observe "globular bodies" that could be specific to cancer tissue was a Belgian physician of German origin, Gottlieb Gluge.[21] In 1837, he published a brief paper on the subject in the *Comptes rendus de l'Académie des sciences de Paris*.[22] His description was, however, extremely vague, and he did not argue that these globular bodies were markers of cancer as such. The real breakthrough for the microscopic anatomy of cancer was the publication of Johannes Müller's famous book, *Ueber den feinern Bau der krankhaften Geschwuelste*,[23] whose main theses quickly spread across European scholarly communities (it was, for instance, translated into English as soon as 1840). In the book, Müller applied the cell theory of his student Schwann to the case of cancer. Under Schwann's approach, the disease was caused by the genesis of abnormal cells out of a cancerous blastema with an altered chemical makeup. These

18 Leland J. Rather, *The Genesis of Cancer: A Study in the History of Ideas* (Baltimore and London: The Johns Hopkins University Press, 1978).

19 Ibid., 62.

20 Louis Mandl, "De la structure intime des tumeurs," *Archives générales de médecine*, 1840, *8*, 313–29, 318–19.

21 Rather, *The Genesis of Cancer*, 83; La Berge, "Debate as Scientific Practice," 426.

22 Gottlieb Gluge, "Recherches sur le fluide contenu dans les cancers encéphaloïdes," *C. R. Acad. Sci.*, Paris, 1837, *4*, 20–21.

23 Johannes Müller, *Ueber den feinern Bau der krankhaften Geschwuelste* (Berlin: Reimer, 1838).

cancer cells possessed the characteristics of embryonic, incompletely differentiated cells, whose anarchic growth was then the cause of tumors.[24] Rather rightly points out that this blastemic conception of cancer was supported during the 1840s and 1850s by most European pathologists who worked on the etiology and symptomatology of tumors.[25] Building on this blastemic theory, Müller added the idea that cancer was an authentically homologous disease that did not put radically new structures into play within the body.[26] He argued that cancer cells were cells that had abnormally returned to their embryonic state. The same thesis was soon advocated also by Virchow,[27] leading him to play a central role in the debates that took place at the Academy of Medicine of Paris.

Both Müller's conception of the nature of cancer tumors and the outlines of Schwann's cell theory were quickly made accessible to a Francophone readership.[28] In 1840, Mandl published in the *Archives générales de médecine* a lengthy account of Müller's work in which he provided details on cell theory. At that time, Mandl believed that the bulk of Schwann's theory had been "demonstrated."[29] He laid special emphasis on the fact that Müller had developed a homomorphus conception of cancer tumors and expressed his own agreement with that conception.[30] In his 1843 *Manuel d'anatomie générale*, Mandl restated his support to Müller's homomorphism,[31] and again spent many pages outlining "the theory of cells," discussing work by Schleiden and Schwann, but also by Jacob Henle and Gabriel Valentin. However, Mandl now had much harsher words about cell theory, which he described as "vague" and "arbitrary."[32] At least when it came to animals, Mandl refused to see the cell as the only element in the composition of tissues. In addition to cells, he thought that fibers also were formed in the blastemic fluid: Mandl and many of his contemporaries accepted the process of blastemic genesis,[33] but simultaneously refused to attribute a prominent role to the cell.[34]

Alongside Mandl's writings, which contributed to the popularization of German-language microscopic anatomy, it is also worth noting that some of the more important texts in the field were quickly translated into French. In 1842, the Strasbourg-based physician, Dominique Auguste Lereboullet, published a partial translation of Schwann's *Mikroskopische Untersuchungen* in the *Annales des Sciences naturelles*.[35] In 1845, Antoine-Jacques-Louis Jourdan, a member of the Academy of Medicine who translated large numbers of books from German into French, published a complete translation of the fourth edition of Müller's *Elements of Physiology*. In the prolegomena,

24 Duchesneau, *Genèse de la théorie cellulaire*, 218–20.
25 Rather, *The Genesis of Cancer*, 95.
26 Lenoir, *The Strategy of Life*, 144.
27 Rather, *The Genesis of Cancer*, 101.
28 Louis Mandl, *Anatomie microscopique*, Tome premier: *Histologie* (Paris: Baillière, 1838–47), 3.
29 Mandl, "De la structure intime des tumeurs," 316.
30 Ibid., 322.
31 Louis Mandl, *Manuel d'anatomie générale* (Paris: Baillière, 1843), 99.
32 Ibid., 79.
33 Ibid., 81, 549.
34 Louis Mandl, *Anatomie microscopique*, Tome second: *Histogenèse* (Paris: Baillière, 1848–57), 355–56.
35 Theodor Schwann, "Recherches microscopiques sur la conformité de structure et d'accroissement des animaux et des plantes," *Ann. Sci. nat., Zoologie*, 1842, *17*, 5–19.

Müller presented the contents of cell theory, which he made sure not to reduce to the blastemic genesis principle alone. Müller particularly emphasized the fact that cells were metabolically active living organisms whose integration could form a higher unit.[36] In 1847, the same translator released, among other publications, a French version of Julius Vogel's treatise on pathological anatomy, which also included a detailed description of cell theory, and in particular of the cytoblastemic mechanism of cell formation.[37]

Thus, even if most Parisian physicians in the 1840s and 1850s did not understand German, they had quick and easy access to the theories and concepts being promulgated by their German counterparts. In particular, the overarching principles of Schwann's cell theory and Müller's theses on the cellular nature of cancer tumors were available in French early in the 1840s. It was in this context of massive diffusion that Hermann Lebert developed his own understanding of the cellularity of cancer.

Hermann Lebert (1813–78) led a very eventful life in Germany, France, and Switzerland.[38] Like Schwann and Virchow, whom he both knew personally, he was first Johann Lukas Schönlein's student. Schönlein convinced him that medicine should draw inspiration from the methodological rigor of the natural sciences. Lebert followed this agenda from the early days of his career and never failed to pay his dues to his teacher.[39] After a first stay in Paris in 1835, Lebert spent most of his winters in the French capital in the early 1840s. During that time, he developed numerous professional relationships with big names in Parisian clinical medicine—including Alfred Velpeau, who provided him with the tumor samples he needed to conduct his microscopic work. Like Donné, Gruby, and Mandl, Lebert taught the techniques of microscopy to physicians. Through his teaching, Lebert also obviously contributed to the diffusion of cell theory. However, he ended up being more influential than Gruby or Mandl, and was soon recognized as the leader of the "Parisian micrographic school."[40] He was quickly able to surround himself with the most promising colleagues and students in the new Parisian school. Four of them stand out: Charles Robin, Aristide Verneuil, Paul Broca, and Eugène Follin. In the 1850s, they formed the core group of this micrographic school, and for a long time—with the notable exception of Robin—they were the first proponents of the idea of the cancer cell. All of them firmly opposed cell theory.

While it makes sense to consider Verneuil, Broca, and Follin as Lebert's disciples, the latter's relationship with Robin can be better characterized as that of two colleagues inspired by the same ambitions and projects. Their first encounter likely dates to August 1844, during a session of the *Société anatomique*.[41] They were then together

36 Johannes Müller, *Manuel de physiologie*, Tome premier (Paris: Baillière, 1845), trans. Antoine-Jacques-Louis Jourdan, 42.

37 Julius Vogel, *Traité d'anatomie pathologique générale* (Paris: Baillière, 1847), trans. Antoine-Jacques-Louis Jourdan.

38 For biographical details, see Hermann Lebert, *Biographische Skizzen und Überblick der von mir bekannt gemachten Werke und kleineren Arbeiten* (Breslau: W.G. Korn, 1869).

39 Hermann Lebert, *Traité d'anatomie pathologique générale et spéciale* (Paris: Baillière, T.1, 1857), 16–17.

40 Paul Broca, *Traité des tumeurs* (Paris: Librairie de la Faculté de médecine, T.1, 1865).

41 La Berge, "Medical Microscopy in Paris," 310.

assigned by the Dean of the Faculty of Medicine to travel to the coast of Normandy and the Jersey Islands to collect specimens of fishes and mollusks in order to enrich the Parisian collections. Thus, their collaboration also extended to the field of natural history for some time.[42] Most importantly, Robin and Lebert participated actively in the foundation of the new *Société de Biologie* in 1848.[43] This society, with its official publication, founded shortly thereafter, the *Comptes rendus de la Société de Biologie*, was for nearly a century one of the most active centers of French biology. It anchored a certain form of positivism and the general refusal of any form of speculation in the field of the life sciences.[44] The physician Pierre Rayer, who went on to become Dean of the Faculty of Medicine, was its first president; Claude Bernard and Charles Robin were the first two vice-presidents. The microscope epitomized the orientation of this new society, which emphasized lab work and experimentation.

The introduction and reception of cell theory in Parisian medicine, mostly revolving around the figure of Lebert, was thus strongly influenced by empiricism and positivism. The precision and accuracy of observation were valued to the detriment of more theoretical and speculative views, which were perceived as too metaphysical. Cell theory was quickly identified with such speculative excesses. It has been well established that Auguste Comte himself was first extremely critical toward theses more or less directly inspired—or perceived to be inspired—by *Naturphilosophie*, like those of Lorenz Oken.[45] In a previous paper, I showed that for several years, Charles Robin expanded on certain aspects of Comte's criticisms, and until the very end refused the biological atomism inherent in cell theory.[46] This philosophical context helps to understand why Lebert and his school would develop and defend the cancer cell concept, in part, in opposition to cell theory.

HERMANN LEBERT AND THE PARISIAN SCHOOL: THE BIRTH OF THE CONCEPT OF CANCER CELL

It was in this general context of renovation of the methods and objectives of medical and biological sciences that Lebert began to tackle the question of the definition and diagnosis of cancer.[47] In 1843, Danish physician Adolph Hannover had suggested that there might be a cancer cell typical of this form of disease.[48] Yet it appears that this

42 Georges Pouchet, *Charles Robin, Sa vie et son œuvre* (Paris: Alcan, 1887), 3.

43 Charles Robin, "Sur la direction que se sont proposée en se réunissant les membres fondateurs de la Société de Biologie pour répondre au titre qu'ils ont choisi," *Comptes rendus de la Société de Biologie*, 1849, *1*, I–XI; Eugène Gley, "La Société de Biologie de 1849 à 1900. Rapport présenté à la séance du cinquantenaire de la Société," *Comptes rendus de la Société de Biologie*, 1899, *51*, 1011–80.

44 Gley, "La Société de Biologie de 1849 à 1900," 1022–23; Eugène Gley, "Influence du positivisme sur le développement des sciences biologiques en France," in *Annales internationales d'histoire: Congrès de Paris 1900, 5^e^ section: Histoire des sciences* (Paris: Armand Collin, 1901), 164–70.

45 Auguste Comte, *Cours de philosophie positive*, Tome troisième, *La philosophie chimique et la philosophie biologique* (Paris: Bachelier, 1838), 530–31; André Stanguennec, "Le scalpel contre le microscope, Auguste Comte et la théorie cellulaire," *Hist. Philos. Life Sci.*, 1984, *6/2*, 171–82.

46 Loison, "Pourquoi refuser la théorie cellulaire?"

47 Hermann Lebert, *Physiologie pathologique ou recherches cliniques, expérimentales et microscopiques sur l'inflammation, la tuberculisation, les tumeurs, la formation du cal, etc.*, Tome premier (Paris: Baillière, 1845), vii–viij.

48 Rather, *The Genesis of Cancer*, 109.

intuition was not followed up, and that Lebert himself heard about it at a later point.[49] Lebert must thus be considered as the main theoretician of the cancer cell concept. On the basis of a considerable volume of observations made over several years in different Parisian hospitals, Lebert progressively refined his conception of general pathology, in which the concept of the cancer cell played a role of choice. The findings of Lebert's research were collected in three successive, French-language publications that stood out in their scope and the unprecedented quality of their iconography (fig. 1): the *Physiologie pathologique* (1845, 2 volumes, 959 pages, and an atlas with 22 plates), the *Traité pratique des maladies cancéreuses* (1851, 892 pages), and the *Traité d'anatomie pathologique* (1857–1861, 2 volumes, 1493 pages, and 2 atlases). These books will allow us to retrace the development of the cancer cell concept.

In 1845, Lebert asserted the necessity of the laboratory sciences (including microscopy) for the continued development of pathological anatomy. However, unlike some of his peers like Müller, Lebert always remained strongly attached to the importance of clinical work.[50] To him, as La Berge emphasized, it was never a question of priority between clinical and microscopic work but of a progressive integration of the two practices.[51] Unlike Müller, again, Lebert saw cancer as an authentically heteromorphous disease, i.e., one with its own ontology.[52] The repeated microscopic analysis of numerous tumor samples taught him that cancer could be identified by the exclusive and clearly specific character of the cancer cell (or globule), which Lebert described in great detail in the first book.[53] The cancer cell stood out primarily because of its enlarged nucleus with clearly visible outlines (fig. 2). It sometimes happened that the cancer globule contained numerous nuclei, forming what was at the time called "mother cells"—a somewhat different meaning than the one it has today. Lastly, the nucleus of the cancer cell, in addition to his characteristic size, generally possessed numerous nucleoli that could also be easily identified.

Turning to the genesis of cancer cells, Lebert set his observations squarely within the blastemic tradition of Müller and Schwann. To him as well, cancer resulted primarily from a chemical alteration of the blastema of blood origin. The nucleus formed first (not, as Schleiden and Schwann maintained, the nucleolus) and then was formed around it, through precipitation, a cell body consolidated from blastema molecules. In the course of the development of a cancer tumor, there was no multiplication of cells, but instead new formations from the continually renewed blastemic fluid.[54] The morphological specificity of the cancer cell was thus the direct consequence of the chemical vitiation of the blastema. If on the one hand, as was commonly believed at the time, the origin of cancer was to be found in the chemical makeup of blastema, and if on the other anatomical elements were actually formed through blastemic

49 Hermann Lebert, *Traité pratique des maladies cancéreuses et des affections confondues avec le cancer* (Paris: Baillière, 1851), 34.
50 Lebert, *Physiologie pathologique*, viij–ix.
51 La Berge, "Dichotomy or Integration?"
52 Hermann Lebert, *Physiologie pathologique ou recherches cliniques, expérimentales et microscopiques sur l'inflammation, la tuberculisation, les tumeurs, la formation du cal, etc.*, Tome second (Paris: Baillière, 1845), 1–2.
53 Ibid., 255–56.
54 Ibid., 257–58.

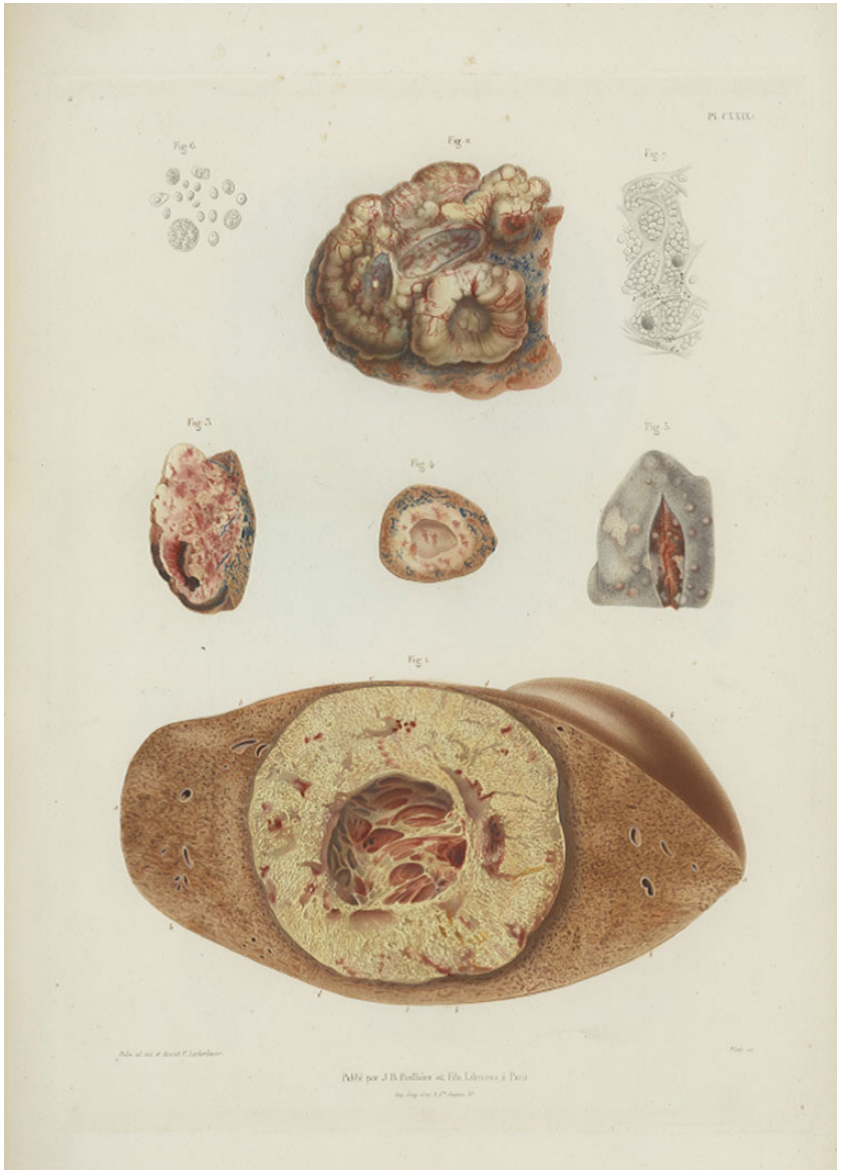

Fig. 1. Plate excerpted from one of Lebert's pathological anatomy atlases, published jointly with his treatises. This depicts the anatomical detail of a cancer of the liver and the lung in a dog up to the cellular level (Lebert 1861, Atlas).

differentiation, then for *theoretical reasons*, it seemed reasonable to think that cancer cells must reflect in form the specific chemistry of the cancerous blastema. Lebert's observations thus fit right in with these explanations.

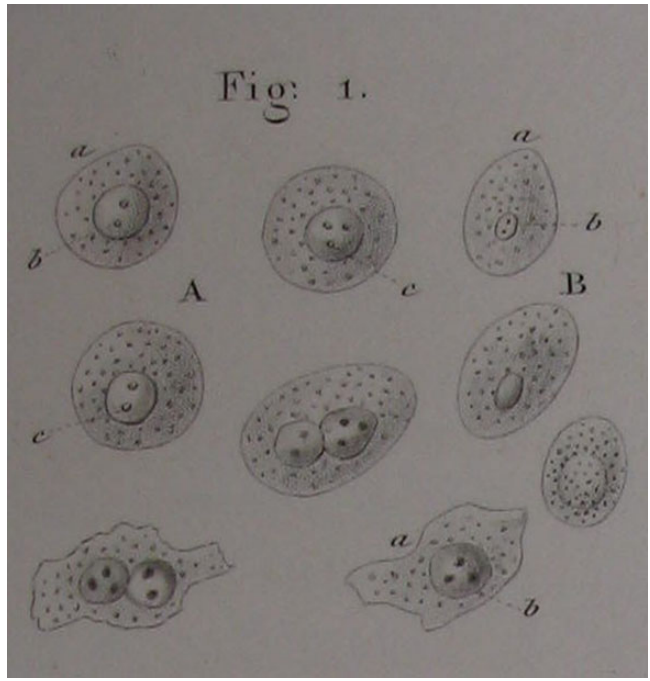

Fig. 2. Hermann Lebert's representation of some typical cancer cells (Lebert 1845).

Following this first publication (1845), part of Lebert and Robin's collaboration focused on the experimental study of the vascularization of cancer tumors. In a series of works that showed a great technical mastery of processes of injection and ligation of blood vessels, Lebert and Robin managed to demonstrate that cancer cells had their own vascularity. This finding strengthened Lebert's belief that cancers should be conceived as parasitic foreign entities, added on to the body's normal physiology.[55]

Lebert used the publication of his *Practical Treatise on Cancerous Diseases* in 1851 as an occasion to make a first review of his work. The book features developments that are virtually identical to the theses he presented already in 1845: the heteromorphism of cancer, the specificity of the cancer cell, and the associated morphological features (including an enlarged nucleus). Lebert added two significant new elements. The first was a somewhat damning critique of German cell theory and its "romantic" offshoots (by which he meant *Naturphilosophie*[56]). At odds with the orthodox proponents of this theory, Lebert argued that all anatomical elements are not of a cellular nature, and he thought it very unlikely that the formation of cells by division was a regular occurrence in animal tissues.[57] In particular, Lebert strongly disputed the theses of Irish physician Walte Walshe (who himself had studied medicine in Paris

55 Lebert, *Traité pratique des maladies cancéreuses*, 38–39.
56 Ibid., 64.
57 Ibid., 64–65.

in the early 1830s) regarding the cellular proliferation of cancer tumors.[58] He restated that cancer cells were new blastemic formations.[59] Lebert also directly targeted the German physicians and naturalists who supported cell theory and who postulated at least potential equivalence between all anatomical elements of the healthy and the pathological body. He called them "unitarists"[60] [*unitaires*]—a term that quickly became anathema to the French micrographic school.

The second new element, which was closely related to this critique of cell theory, was the promotion of French microscopy and its support for the cancer cell concept. While Lebert conceded that his colleagues outside of France, like Vogel, Bennett, and Virchow, doubted the validity of the concept of the heteromorphism, he emphasized that his theses enjoyed a much better reception in Paris.[61] In the book, Lebert also posed a distinction between the detailed, empirical French style of science and the more speculative German science, which was still subservient to *Naturphilosophie*. This distinction allowed him to downplay criticisms that had since 1845 been voiced against him concerning the value of the observation of so-called cancer cells for the diagnosis of cancer.

As we will see (the third section), the years 1852 and 1854–55 were then marked by long and heated debates on these questions among the Parisian medical community. During the same period, thanks to Remak and then Virchow, the principle of cell division became an important component of the renewed cell theory.[62] When Lebert published the two volumes of his third treatise later in 1857 and in 1861, the academic and theoretical landscape had experienced major changes, and Lebert positioned himself in light of these changes.

He did this in the first pages of the first volume by acknowledging that *Naturphilosophie* might also have played a positive role in the rise of the life sciences.[63] Then he did so by very harshly criticizing the clinicians—whom he called "backward minds"—for allegedly stubbornly refusing to use new technologies in pathological anatomy, starting with the microscope.[64] Yet Lebert stuck by the substance of his previous works and reasserted the value and importance of the cancer cell. Again he emphasized the specificity of its morphology[65] (see fig. 3) and its blastemic formation from vitiated blood.[66]

It was in the second volume of his *Treatise on Pathological Anatomy* that Lebert ended up rethinking some of his conceptions most radically. Drawing on findings made by Remak, Virchow, and His, and on his own work, Lebert renounced Schwann's

58 Walte Walshe, *The Nature and Treatment of Cancer* (London: Taylor and Walton, 1846).
59 Lebert, *Traité pratique des maladies cancéreuses*, 65–66.
60 Ibid., 162.
61 Ibid., 15–16, 34–35.
62 Harris, *The Birth of the Cell*, 128–37.
63 Hermann Lebert, *Traité d'anatomie pathologique générale et spéciale, Ou description et iconographie des altérations morbides tant liquides que solides observées dans le corps humain*, Tome premier (Paris: Baillière, 1857), 16.
64 Ibid., 17.
65 Ibid., 279–80.
66 Ibid., 290–91.

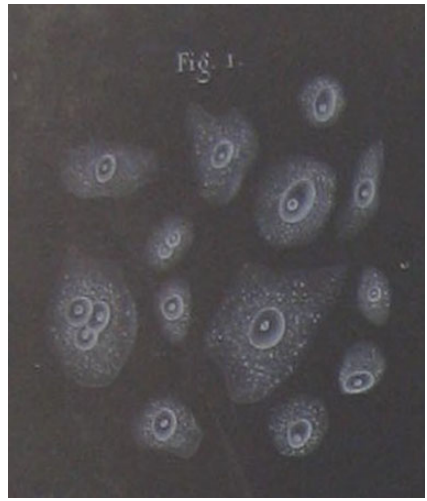

Fig. 3. Hermann Lebert's representation of a few cells extracted from a rectum cancer in a deceased patient (Lebert 1857).

cytoblastemic hypothesis, which he now dismissed as a "dogma" that needed to be put to rest.[67] Furthermore, Lebert noted that he had invested time in the detailed study of the stages of cell division and discussed his own observations, drawn in part from the study of cartilage cells. He provided a very detailed diagram representing this process, in which he clearly identified the main stages of what would be called mitosis some fifteen years later (fig. 4).

Again, it is important to emphasize the necessity of a clear distinction between the mechanism of cell formation and the postulate of atomism that constituted the core of cell theory. The latter, which remained unchanged from Schwann to Virchow, consisted in the idea that the body is made up of physiologically autonomous units—cells. In this sense, the mechanism of cell genesis is nonessential. One could very well subscribe to Schwann's theses on the blastemic formation of cells and at the same time reject cell theory, as Mandl and Lebert did, not to mention many European physicians during the 1840s. Lebert's conversion to the Virchowian principle of *omnis cellula e cellula* did not lead him to embrace cell theory as a whole. In 1861, Lebert continued to see the cell not as the basic element of the living organism but as one hierarchical level among others in its structure.[68] Like Robin, Lebert still devoted all his attention to the chemistry of organic fluids.[69]

While Lebert's support for the mechanism of cell division did not force him to change his stance on cellular atomism, it still raised an additional challenge to the

67 Hermann Lebert, *Traité d'anatomie pathologique générale et spéciale, Ou description et iconographie des altérations morbides tant liquides que solides observées dans le corps humain*, Tome second (Paris: Baillière, 1857), 669–70.

68 Ibid., 662.

69 Loison, "Pourquoi refuser la théorie cellulaire?"

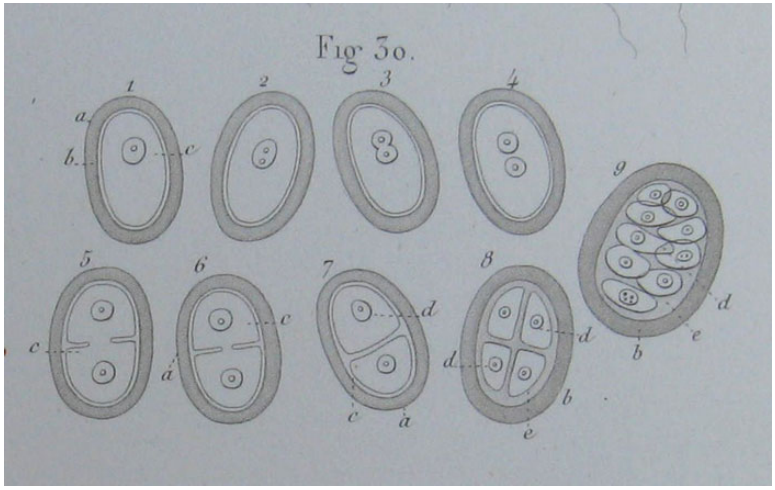

Fig. 4. Diagram on the stages of cell division for a cartilage cell. Lebert already distinguished between the division of the nucleus and the division of the cell (Lebert 1861).

concept of the cancer cell. Indeed, as we have seen, the blastemic hypothesis provided an interpretative framework for conceiving how a given fluid could give birth to new anatomical elements with a specific morphology. Conversely, for Virchow, the necessarily cellular origin of all forms of tumors had become an argument in support of the homomorphism of pathologies, including cancer.[70] Lebert would not give up on the specificity of the cancer cell and on his interest in diagnosis.[71] Admittedly, he conceded that the pathological state was only a change in physiological state, and that this removed "all ontological boundary" between health and disease. However, if cancer cells directly derived from the division of pre-existing cells—probably those of the connective tissue, as in Virchow—they did so in an entirely pathological manner, i.e., "outside of their usual mode of propagation."[72] The reader may feel distinctly Lebert's embarrassment, as his position was undeniably weakened by the loss of support from blastemic mechanism. Yet he still defended the relevance—at least for descriptive purposes—of the cancer cell concept.

CANCER CELL VERSUS CELL THEORY. RETHINKING THE OPPOSITION BETWEEN MICROSCOPISTS AND CLINICIANS IN PARIS

Between January 1844 and January 1855, no less than three particularly long and intense debates took place in Paris regarding the diagnosis and curability of cancer. The last of the three debates, at the Academy of Medicine, is already known by

70 Rudolf Virchow, *La pathologie cellulaire basée sur l'étude physiologique des tissus* (Paris: Baillière, 1861), trans. Paul Picard.

71 Lebert, *Traité d'anatomie pathologique*, 675.

72 Ibid., 673.

historians of science: Ackerknecht and especially La Berge have shown how the study of such controversies yields insight into the practice of science in the nineteenth century.[73] This section offers a different approach to these debates, with a focus on their contents and outcomes regarding cell theory and the cancer cell concept. As I pointed out in the introduction, the fact that at least two of these debates turned on the question of the relevance of the cancer cell concept made them occasions for expressing stances on cell theory. This section is dedicated to the analysis of these stances.

The first debate took place at the Academy of Medicine between January 9 and March 26, 1844, and was documented in a series of transcripts published in the *Bulletin de l'Académie de médecine*.[74] On the initiative of Jean Cruveilhier, it consisted in questioning the possible morphological specificity of breast cancer in women and distinguishing it from noncancerous "fibrous bodies" whose removal was unnecessary. Of the three debates, this one is the simplest to analyze, because while it did involve some controversy (mainly between Cruveilhier and Roux), it did not concern the use of the microscope or cell theory. The question of the microscope was surprisingly peripheral; only on a few rare occasions did protagonists like Rochoux offer regret that the device had been underused in the investigation of such morphological questions.[75] Cruveilhier himself claimed that he did not have the "leisure to have recourse to this supplement of light" offered by the microscope.[76] Later, Roux still wondered whether it would be possible to "usefully combine microscopic observation and chemical analyses with the usual resources of anatomy and known processes in pathological anatomy."[77] The first lesson to be learned from this debate is that, to date, the use of the microscope remained a largely exceptional practice for Parisian physicians who studied the pathological anatomy of cancer.

The same observation applies to cell theory and Schwann and Müller's theses. Remarkably and significantly, only Velpeau acknowledged micrographic research by Vogel, Müller, and Mandl (at the time Velpeau collaborated with the latter on a regular basis). For Velpeau—who went on to become the main opponent of the cancer cell concept—in 1844 cancer tumors were distinguishable under the microscope from fibrous tumors because "cells" and "corpuscles" were visible instead of "fibers and fibrils."[78] At the time, Velpeau thus attributed a measure of morphological specificity to cancer, even though he hastened to add that this did not necessarily facilitate diagnosis. As the end of the debate neared, he spoke out for the second time in more explicit terms. He added Lebert to the list of names he cited (the only occurrence of Lebert's name throughout the debate) and mentioned having himself verified that "cancerous matter is always found in the form of vesicles or cells in the so-called cancerous tissues, while other tumors only display flakes or fibrils under the

73 La Berge, "Debate as Scientific Practice."
74 *Bulletin de l'Académie de médecine*, 1843–44, *9*, 330–653.
75 Ibid., 357.
76 Ibid., 366.
77 Ibid., 388.
78 Ibid., 361.

microscope."[79] Lastly, it is worth noting that, in a fashion similar to Velpeau, Blandin too explained that during a collaborative study with Mandl on a mammary tumor, he had managed to observe "corpuscles of cancerous matter"—providing, however, no further information on the subject.[80]

The bulk of the 1844 debate, which lasted nearly three months and is recounted over several hundreds of pages, did not concern microscopy or cell theory. This would change a few years later. From November 13, 1852, to January 5, 1853, a second debate on cancer diagnosis took place at the Society of Surgery of Paris; this time the use of the microscope and the value of the cancer cell concept were core concerns.[81] After his 1845 and 1851 publications, Lebert's own theses were now well known in France and abroad and were hotly debated. Most of the debate consisted in a standoff between Lebert and René Marjolin, the Secretary-General of the Society, who was on that occasion the spokesman for clinicians. At odds with Lebert's school, Marjolin asserted the possibility of tissue degeneration, i.e., the transformation of a healthy tissue into a cancerous tumor, not necessarily endowed with specific cancer cells. In other words, Marjolin supported the idea of the homophormism of cancer. Lebert, who made sure to present himself as a physician and not as a microscopist,[82] stressed the need to introduce laboratory techniques into the field of pathological anatomy. He firmly, sometimes even harshly,[83] demanded that clinicians finally make room for microscopy in their practice. Within a few years, in a period that saw Lebert's first two publications, the terms of the debate changed radically: microscopy and the nascent cytology were now central issues.

It was also then that Velpeau began to distance himself from Lebert and his cancer cell concept. In 1854, a few months before the third and last debate, he published his *Traité des maladies du sein et de la région mammaire*, a comprehensive volume that compiled several decades' worth of anatomo-clinical observation. While he admitted that the cancer cell and the microscope could be of help to the diagnosis,[84] Velpeau did not agree that this cell could be an absolute and sufficient criterion and reasserted the primacy of clinical examination over micrographic inspection. This was exactly how the last standoff between clinicians and microscopists began—again at the Academy of Medicine in Paris. It would be the longest one, lasting from September 26, 1854, to January 16, 1855.[85] Nearly twenty protagonists were directly or indirectly involved in this last debate, including Rudolf Virchow.

The first essential point that needs emphasizing is the great imbalance between the parties. As La Berge perceptively remarked, no genuine microscopist was directly involved in the debate.[86] Most of the first-generation microscopists (Donné, Gruby, Mandl) had moved on to something else (Donné, Gruby, Mandl). Lebert, for his

79 Ibid., 639.
80 Ibid., 518.
81 *Bulletin de la Société de chirurgie de Paris*, 1852–53, 3, 232–356.
82 Ibid., 314.
83 Ibid., 350.
84 Alfred Velpeau, *Traité des maladies du sein et de la région mammaire* (Paris: Masson, 1854), XV–XVI.
85 *Bulletin de l'Académie de médecine*, 1854–55, *19*, 7–447.
86 La Berge, "Debate as Scientific Practice," 431–32.

part, was no longer in Paris, and was never a member of the Academy anyway. The representatives of the young Parisian school (Robin, Follin, Broca, Verneuil) were precisely too young to get involved; they turned to a variety of medical journals to report on these exchanges, often very openly giving their opinions on these matters.[87] Within the Academy's walls, the debate was not a direct opposition between clinicians and microscopists; it was chiefly a debate among clinician surgeons, between those who supported the systematic use of the microscope and the vast majority who saw it as an inessential additional tool.

As in 1852, but this time on the initiative of Velpeau himself, the debate focused on the use of the microscope and the reliability of the cancer cell criterion in diagnosis. Nevertheless, unlike two years before, references to German-language cell theory and anatomy were now ubiquitous, and even decisive in the outcome. The clinicians who argued that microscopic examination was not necessary indeed embraced cell theory somewhat opportunistically because it allowed them to support the homomorphism of cancer and the primacy of clinical work in diagnosis. The name of Schwann—sometimes misspelled[88]—came up from time to time during the debate. More frequently cited, the names of Müller, Bennett, Vogel, and Virchow were used to cement the position of the Parisian clinicians against the specificity of the cancer cell.[89] Cell theory, which was again called "unitary,"[90] asserted the at-least partial equivalence of cells within the body and accordingly the impossibility of true heteromorphism.

This theoretical setting ultimately resulted in a highly unexpected situation: the clinicians who supported the microscope fought cell theory, whereas those who resisted the use of the microscope now promoted the theory. For example, on several occasions, the famous veterinarian Onésime Delafond used Schwann, Müller, and Virchow's cell theory as a decisive and definitive argument against Lebert's stance.[91]

Yet, all the protagonists agreed on one important point: the blastemic genesis of anatomical elements. According to some, the cancerous blastema had an undetectable "morbid principle" and the resulting cells bore nothing specific.[92] In their view, this meant that clinical work should be given the first role in cancer diagnosis.[93] Others, who were fewer in number, concurred with Lebert in contending that the cancerous blastema was organized into typical cancer cells, whose characteristic features could be seen under the microscope. Despite this divergence, Schwann's cytoblastemic mechanism faced no opponents at the time.

Beyond the confines of the Academy of Medicine, the debate had also spread to various medical journals (*Moniteur des hôpitaux*, *Gazette hebdomadaire de médecine et de chirurgie*, *Archives générales de médecine*).[94] Lebert's disciples showed a steadfast support to his conceptions as well as a great deal of combativeness towards the

87 Ibid., 433–34.
88 *Bulletin de l'Académie de médecine*, 160.
89 See, for example, ibid., 246.
90 Ibid., 357.
91 Ibid., 388.
92 Ibid., 405.
93 Ibid., 441–43.
94 La Berge, "Debate as Scientific Practice," 433.

Academy, which they saw as a fossilized institution. Verneuil, for instance, emphatically called his young colleagues to "loyally defend the flag of the scientific school to which we are proud to belong."[95] "Unitary" cell theory was combatted as extravagant and unfounded (and therefore "German") speculation, whereas the heteromorphism of cancer was reasserted. Lastly, in a fourth medical periodical, the *Gazette hebdomadaire médicale*, Virchow intervened toward the end of the debates, on February 16, 1855. He published a letter translated into French, *Opinion sur la valeur du microscope*. In it, Virchow expressed in very explicit terms his support and lent the weight of his authority to the clinicians who fought Lebert's theses. Emphasizing his newfound skepticism toward the cytoblastemic mechanism, he "strongly rejected the specificity of the pathological cell."[96]

This succession of debates shows that the reception of cell theory in Parisian medicine was marked by an extremely controversial atmosphere. Introduced by the first generation of microscopists, starting with Mandl and Lebert, the conceptions of Müller, Schwann, and then Virchow were subsequently used by clinicians as arguments against the cancer cell concept and the supremacy of the microscope. In Paris, in the field of medical disciplines, cell theory was ultimately a means much more than an end: it attested to clinicians that the homomorphism of cancer was well founded, and in doing so gave legitimacy to their practice.

EPILOGUE: DECLINE AND DEATH OF THE CANCER CELL CONCEPT

One of the conclusions of La Berge's analysis of the 1854–55 debate at the Academy of Medicine was that it ended in status quo.[97] This reflects the impetus of her paper, which was to understand the implicit stakes of the *practice* of debate in nineteenth-century Parisian science. This paper argues instead that this debate did have a winner and that for a very long time, the outcome of the debate helped to discredit the idea that cancer was a pathology of its own with distinct features, starting with the cancer cell.

As La Berge notes[98] without further examination, the debate first had an official resolution, since the Academy quickly organized competitions on the two questions that underpinned the oppositions: the value of the microscope for cancer diagnosis and the curability of cancer. Strasbourg researcher Eugène Michel received a prize on that occasion, and his findings were published in 1857 in the *Mémoires de l'Académie de médecine*.[99] Michel was a member of the micrographic school of Strasbourg, where cell theory had been received much more positively than in Paris during the 1840–70 period, partly thanks to the teachings of Emile Küss.[100] He had already been a

95 Aristide Verneuil, "Le microscope et le cancer devant l'Académie de médecine—Etat de la discussion," *Gazette hebdomadaire de médecine et de chirurgie*, 1855, *2*, 65–70, 70.

96 Rudolf Virchow, "Opinion sur la valeur du microscope," *Gazette hebdomadaire médicale*, 1855, *2*, 124–26, 125.

97 La Berge, "Debate as Scientific Practice."

98 Ibid., 449.

99 Eugène Michel, "Du microscope, de ses applications à l'anatomie pathologique, au diagnostic et au traitement des maladies," *Mémoires de l'Académie de médecine*, 1857, *21*, 241–437.

100 Marc Klein, "Sur les débuts de la théorie cellulaire en France," *Thalès*, 1951, *6*, 25–36.

member of the Strasbourg school for a long time when he published his nearly two-hundred-page long dissertation entitled *Du microscope, de ses applications à l'anatomie pathologique, au diagnostic et au traitement des maladies*. By his own admission, he had begun work on it in 1848, a few years after the beginning of the researches conducted by Lebert in Paris. As could be expected, Michel argued throughout against the specificity of the cancer cell, drawing on cell theory.[101] He very clearly stated that the Strasbourg and Würzburg (Virchow) schools had the "honor of having been first to fight for the new doctrine [the homomorphism of cancer]."[102] Michel's book is unequivocal: he proves the clinicians right and the microscopists of the Paris school wrong.

It was in this context that the 1861 French translation of Virchow's *Cellular Pathology* appeared. The translator Paul Picard was himself a physician and had been Virchow's student. He added to the original text an introduction written in the fall of 1860. On the very first page, Picard looked back on the 1854–55 debate and noted in no uncertain terms that "the German micrographic school provided weapons to fight and to *defeat* French microscopists."[103] On a few occasions, Virchow himself pointed out his support for the homomorphism of cancer and his opposition to what he called the "West's micrographic schools."[104] *Cellular Pathology,* the key text of the "second" cell theory, was therefore received in a very special context in Paris, as it confirmed the defeat of Lebert and his micrographic school.

During the 1860s, the decline of the cancer cell concept was also reflected in the evolution of the ideas of some members of the Parisian school itself. Charles Robin, who was for some time Lebert's closest collaborator in Paris, repudiated it fairly quickly, between the late 1850s and the early 1860s. In 1855, in the "Cancer" entry of the medical dictionary that he published with Emile Littré, Robin still wrote, inspired by Lebert, that "one gives the name of *cancerous anatomical element* or *cancer* (*cancerous cell* and *nuclei*) to a species of anatomical element characterized by its state [. . .] [and] a unique aspect that none of the normal elements of the economy offer."[105] Ten years later, in an updated edition of the same dictionary, not only was there no longer any mention of the cancer cell, but the concept of cancer itself was denied any ontological content; the entry even claimed that the word should now "be rejected, like all those words which are attached to a false idea, as using them always tends to remind one of that idea."[106]

The following year, Victor Cornil, Louis Ranvier's main collaborator and a future professor of pathological anatomy at the Faculty of Medicine of Paris, published a book entitled *Du cancer et ses caractères anatomiques*. In 1865, this research had been awarded the prestigious Portal prize of the Academy of Medicine; once again it presented

101 Michel, "Du microscope," 247.
102 Ibid., 248.
103 Paul Picard, "Introduction," in Virchow, *La pathologie cellulaire*, V, my emphasis.
104 Ibid., 52, 53–54.
105 Emile Littré and Charles Robin, *Dictionnaire de médecine, de chirurgie, de pharmacie, des sciences accessoires et de l'art vétérinaire de P.-H. Nysten* (Paris: Baillière, 1855), 200.
106 Emile Littré and Charles Robin, *Dictionnaire de médecine, de chirurgie, de pharmacie, des sciences accessoires et de l'art vétérinaire de P.-H. Nysten* (Paris: Baillière, 1865), 211.

Lebert's theses as outdated.[107] Unlike Robin, who remained an opponent of cell theory until the very end, this refusal of the anatomical specificity of cancer did come both for Cornil and for Ranvier with an unequivocal support to cell theory and its biological atomism. Both viewed the cell as "the organic unit *par excellence*."[108] According to Cornil, in 1865, only three physicians in Europe remained convinced of the value of the cancer cell concept: Lebert and two of his disciples, Broca and Follin.[109]

In the 1870s and 1880s, the cancer cell concept was already viewed as an obsolete milestone in the history of medicine. In 1885, Amédée Dechambre, Mathias Duval (a student of Küss), and Léon Lereboullet referred to it in the past tense in the "Cancer" entry of their famous *Dictionnaire usuel des sciences médicales*.[110] Like Robin, they thought that "in the future, the word [cancer would] disappear," as it encompassed a range of pathologies that could be characterized in clinical terms but had no common basis in anatomical terms.[111] Lastly, in his widely distributed *Traité d'anatomie pathologique générale*, Raymond Tripier recalled in the early twentieth century that Virchow's work led to the "permanent rejection of the specificity of the cancer cell."[112]

Overall, in the field of medical sciences, the second half of the nineteenth century was largely dominated by the postulate of ontological equivalence between the healthy and the pathological state.[113] This postulate was a core feature in the theses of Virchow, Bernard, Robin, and Lebert himself, and ultimately became an insurmountable obstacle for the cancer cell concept.

CONCLUSION

Two important findings pertaining to the history of nineteenth-century cell theory can be drawn from this study. First, it has shown that the ideas developed in Germany by Müller, Schleiden, and Schwann were accessible, known, and implemented in the field of Parisian medicine within a very short span of time. This reception involved more than only anatomical microscopists, since clinical surgeons opportunistically used cell theory—admittedly later—as a *pro domo* argument during the famous 1854–55 debate at the *Académie de médecine*. It is also worth noting that this reception, unlike, for instance, that of Darwinism later,[114] was generally characterized by an excellent understanding of the competing theses. Thus, a distinction between the acceptance of a mechanism of cell genesis and of the postulate of biological atomism was well established, since to my knowledge, during the 1840–55 period, no physician in France opposed the idea of the blastemic genesis of anatomical elements, whereas

107 Victor Cornil, *Du cancer et de ses caractères anatomiques* (Paris: Baillière, 1866), 303–4.
108 Victor Cornil and Louis Ranvier, *Manuel d'histologie pathologique*, Tome premier (Paris: Baillière, 1869), 1.
109 Cornil, *Du cancer*, 303–4.
110 Amédée Dechambre, Mathias Duval, and Léon Lereboullet, *Dictionnaire usuel des sciences médicales* (Paris: Masson, 1885), 244.
111 Idem.
112 Raymond Tripier, *Traité d'anatomie pathologique générale* (Paris: Masson, 1904), 658.
113 Georges Canguilhem, *The Normal and the Pathological* (New York: Zone Books, 1991). Translation by Carolyn R. Fawcett and Robert S. Cohen.
114 Conry, *La réception du darwinisme en France*.

many of them fought the biological atomism of cell theory because it conferred a special value on the cell in the anatomical hierarchy of organisms.

Secondly, and perhaps more fundamentally, it now seems undeniable that the cancer cell concept was constructed through its opposition to cell theory. Further, this concept constituted a real challenge to the theory, especially since it was based on a wide range of high-quality observations. The intrinsic quality of the research conducted by the Paris micrographic school indeed deserves emphasis. The minute and carefully documented descriptions of the morphological attributes of the cancer cell produced by these physicians during the 1840s and 1850s remain valuable today and are still printed identically in all pathological anatomy handbooks.[115] After the decline of the cancer cell concept and its outright abandonment in the second half of the nineteenth century, it was reformed independently—with no connection to Lebert's work—during efforts made in the 1930s and 1940s to develop reliable screening tests for cervical cancer.[116] Only very recently was Lebert's pioneering work in pathological anatomy rediscovered and its value recognized.[117] A 2014 scientific paper, for instance, claims that "the diagnostic parameters employed are still largely morphological and nucleus centric, essentially the same type of features that cytologists have been looking at for the past 160 years."[118]

Consequently, at least as far as the microscopic anatomy of cancer is concerned, cell theory, instead of being a natural extension of the use of the microscope, was actually hindered and contested on the basis of findings from microscopic works currently still regarded as valid. In this sense, it was really a theory from the start—i.e., an abstraction, not simply an empirical induction relying too narrowly on the unproblematic observation of nature.

ACKNOWLEDGMENTS

I owe special thanks to Marion Thomas for her advice at various stages in the writing of this text. I would also like to thank Christopher Crenner for his support throughout the review process and the two referees for their helpful comments.

FUNDING

This paper was translated from French by Jean-Yves Bart and received support from the Excellence Initiative of the University of Strasbourg, funded by the French government's Future Investments program. The findings presented here are outcomes of the Franco-German ANR-DFG "POLCELL" project (University of Strasbourg, University of Braunschweig) examining the genesis of cell theory in nineteenth-century France and Germany.

115 Alan Stevens, James S. Love, and Barbara Young, *Wheater's Basic Histopathology* (Churchill Livingstone: Elsevier Science Limited, 2002).

116 George N. Papanicolaou, "A New Procedure for Staining Vaginal Smears," *Science*, 1942, *95/2469*, 438–39.

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