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# SHIFTING SCALES, ARTICULATING CANCER: TOWARDS A CARTOGRAPHY OF ONCOBIOLOGICAL RESEARCH*

## Abstract

The "molecular turn" in cancer research has often been associated with a reductionist program, which would attempt to locate the origin of the initiation, promotion or suppression of tumours in genetic processes. Researchers in oncobiology, however, still struggle with the problem of having to deal with diseases which are mostly caused by exposure to environmental factors. Whereas the processes dealt with by molecular genetics are seen as crucial to the understanding of cancer, just how these are connected to transformations at the cellular, tissue, organ, system or organismic level and to interfaces with the environment is still one of the major challenges to oncobiology. Drawing on the laboratory practice and on the discourse of oncobiological researchers, it is argued that a specific mode of spatial imagery, centered on scale, is one of the resources these researchers draw upon in order to articulate the different levels at which cancer is located by the various approaches and disciplines involved. This feature is central to the emergence of a new *contextual* paradigm in oncobiology.

Adapting an analytical tool developed by Boaventura de Sousa Santos for the study of law, a cartographic approach to cancer research is outlined and drawn upon to discuss work in progress in an oncobiology laboratory. This framework is based on the centrality of scale and on the definition, construction and articulation of scientific work and of scientific objects at different scales.

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The history of molecular biology, of the redefinition of cancer as a genetic disease and of the role of molecular biological approaches and biotechnology in that redefinition has been the object of recent, detailed historical and ethnographic research[1]. Work on these processes in countries like the United States, France or Spain suggests that conditions pertaining to the differing national organization of scientific and medical professions, disciplines and specialties and to specific, local features of research units may give rise to different ways in which research in molecular genetics is organized and incorporated into cancer research. Work in progress on a cancer research institute in Portugal provides additional support for the need to widen the scope and complexify the picture of comparative work in this area. Three interesting features stand out in the Portuguese case:

a) nationally specific characteristics related to disciplinary and professional histories are central to an understanding of the particular ways in which molecular genetics was incorporated into cancer research and contributed to its transformation over the last two decades;

b) these national specificities, however, are strongly linked, on the one hand, to local arrangements in research units, related to the training of the researchers, to the way different disciplinary approaches are articulated and to the specificity of

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[1]In a review of recent work on the history of molecular biology, Abir-Am (1995) called for a greater attention to the transnational and "multisite" settings in which molecular biology developed. For relevant contributions to both the history of molecular biology and the relationship between molecular biology and cancer research along that line, see Gaudillière, 1992, 1993a, b, 1994, 1996; Craeger and Gaudillière, 1996; Löwy, 1990, 1997. Work by Joan Fujimura (1987, 1992, 1995, 1996) has explored in great detail the "molecularization" and geneticization" of cancer in the United States. The role of molecular biological approaches in the politics of cancer in the United States is dealt with iin Proctor, 1995. Santesmases and Muñoz (1997a,b) offer an interesting account of how molecular biology developed in the peripheral scientific world of Spain, providing a particularly relevant case for a comparison with Portugal. For a brief outline of the introduction and spread of molecular biology and biotechnology in Portugal until the early 1990s, see several of the contributions to Gago (ed.), 1992.

particular research subjects, and, on the other hand, to the transnational links of research units and of their members, as expressed in the privileged relationships with other units abroad for graduate training and cooperative research;

c) finally, molecular biological approaches have been - and still are - crucial to the articulation of research on "local" types of cancer to "global" scientific themes and concerns, and to the insertion of researchers in transnational science worlds.

The "molecular turn" in cancer research has often been associated with a program resting upon what Stephen Jay Gould called, in a review of Richard Dawkins's *The Selfish Gene*, the "bad habits of Western scientific thought", based on atomism, reductionism and determinism, the "idea that wholes should be understood by decomposition into basic units; that properties of microscopic units can generate and explain the behavior of macroscopic results; that all events and causes have definite, predictable, determined causes" (Gould, 1983: 77). It will not be surprising that the attempts at looking for the ultimate location of the factors related to the initiation, promotion or supression of tumours in the genes are particularly vulnerable to this criticism. As Fujimura (1996: 266-267, note 1) noticed, however, "[m]olecular biological cancer research occupies only part of the vast cancer research world", even if it has become a particularly influential approach. Its association with the aforementioned "bad habits" of atomism, reductionism and determinism depends on how it relates to other approaches and to the way "cancer" is constructed as a heterogeneous object linked to a diversity of scientific perspectives. This point is particularly relevant in settings where the rise of molecular genetics, even if significant, did not displace other approaches, but rather offered new opportunities for articulating different ways of studying cancer. In fact, in spite of the breakthroughs in the understanding of the biology of cancer which molecular biology allowed, researchers in oncobiology still struggle with the problem of having to deal with diseases whose links to exposure to environmental

factors are cerucial. Whereas the processes dealt with by molecular genetics are seen as central to the understanding of cancer, just how these are connected to transformations at the cellular, tissue, organ, system or organismic level and to interfaces with the environment is still one of the major challenges to oncobiology. The complexity and heterogeneity of oncobiological processes is linked to the recognition, by researchers, of the centrality of *scale* in representing cancer and to the attempt at articulating what some scientists describe as an emergent *contextual paradigm* in oncobiology[2].

This paper discusses the way different uses of molecular biological approaches and techniques in a cancer research laboratory in Portugal are made part of a "style" of research which articulates the emerging contextual paradigm. As this case suggests, this requires a renewed understanding of the way representations of cancer, the organization of oncobiological research and the geopolitics of research on cancer and molecular biology are related and co-constructed. Due to its central use of the concept of scale, cartography - the art of making maps at given scales - provides an interesting language to deal with these issues[3].

## 1. Scale matters: towards a cartography of cancer

In an innovative approach to the sociology of law, Boaventura de Sousa Santos (1995) argued the need to develop analytic approaches to phenomena for

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[2]The expression "contextual paradigm" is used by the researchers themselves, and will be retained throughout this paper. It would perhaps be preferable to call it a "transaction zone" (Galison, 1996) or, at best, a "creole zone" (Löwy, 1992: 374) rather than a paradigm, since, as will be argued in later sections, what is at stake here is a loose articulation of a diversity of approaches whose commensurability cannot be taken for granted.

[3]For detailed discussions of this approach, see Santos, 1995: 456-473, and Nunes, 1996d. For a different use of spatial images in science studies see Mol and Law, 1994.

which scale is a central dimension. Cartography, the art of making maps according to the scale at which a given territory is to be represented, provided more than an useful analogy. It offers a set of heuristic instruments for the exploration of research objects requiring a focus on scale, as is the case of cancer and cancer research.

Cartographic map-making involves three types of dimensions, associated with three corresponding sets of operations: scale, projection and symbolization. Rather than going through a detailed explanation of these dimensions, I shall discuss their relevance for the study of the world of cancer research.

Cancer is a feared disease[4], above all, because of the way it expands within a given organism. A local deregulation of cell growth turns more or less rapidly into a proliferation of deregulated cells, spreading to neighbouring tissues and soon affecting the organism as a whole. The development of cancer is a process involving changes of scale: a localized, cell-, tissue- or organ-specific problem grows into a global, organism-wide deregulation. This seems to be true of the variety of ways cancer is defined and constructed in research and clinical practice: as the result of environmental aggression to an organism; as an interaction between a pathogenic agent and a host - the human organism-; as a disease of organs or systems; as a deregulation of cellular activity in tissues; as a transformation in molecular processes. Different research orientations and different research objects will be constructed depending on the scale chosen. This in turn, is linked to the different scales on which the transdisciplinary world of cancer research is organized. The closer we get to the molecular definition of research objects, the more "do-able" the translocalization of research results will be, since objects at that

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[4]Cancer is, in fact, a set of heterogeneous diseases which have in common a process of deregulation of cell growth. Whenever necessary for clarifying my argument, I shall distinguish between different types of cancer. When dealing with common features of cancers, as in this paragraph, I shall treat it as a single disease. For a highly readable (for non-specialists) introductory presentation and discussion of the biology of cancer with a focus on the centrality of genetics by two of the most prominent figures in the field, see Varmus and Weinberg, 1993. In 1989, Varmus was awarded the Nobel prize in Physiology or Medicine, with J. Michael Bishop, for his work on retroviruses and oncogenes.

particular scale are more likely to be deterritorialized and disembodied, that is, to have the weakest links to specific organisms or contexts. Molecular objects are thus more easily reappropriated beyond the specific context of their production, be it a disciplinary context or a territorial context, and more likely to be standardized than objects which carry with them the traces of their messy origin in organisms or specific local conditions. Scientists working at this scale have more opportunities and an easier task to become part of mainstream research programs or research orientations at a global level. In the case of cancer research, as was already mentioned, some types of cancer are regarded as cancers with a peculiarly local expression, while other types, which are common in core countries and are considered as particularly threatening there, are defined as global health problems. The funding of research, diagnosis and therapy, as well as the definitions of the relevant research problems in this field and, consequently, access to international publications and scientific fora and scientific reputations tend to follow the distribution of types of cancer into "global" and "central" (like breast cancer) and "local" or "peripheral" (like stomach cancer)[5].

Scale thus appears as a central dimension for the understanding of cancer as a disease and as an object of research, as well as for dealing with the organization and dynamics of cancer research and of its geopolitics. The move towards a contextual paradigm in oncobiology requires an engagement with cancer as a multiscale and multifactorial process. This, in turn, raises the problem of how to make apparently incommensurable approaches to cancer research compatible or, at least, how to define a "trading zone" where this multiscale and multifactorial, context-sensitive approach to cancer may be negotiated by the actors involved.

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[5]Fujimura (1987) suggests a different approach to the centrality of scale in cancer research, by focusing on the processes of *alignment* and *articulation*. Alignment refers to the way actors and resources located on the same scale get their work done, whereas articulation focuses on the relationships and adjustments between scales - the experimental setting, the laboratory and the social worlds involved.

An interesting consequence of this move is the need to locate the scale at which actors construct and represent the phenomena that are relevant to their work, but also the ways in which they reduce objects at different scales to one and the same scale, thus allowing them to be manipulated, recombined and transformed. As Santos (1995) puts it, the scale at which action takes place is always *local* for the actors involved. From an ethnomethodological perspective, Michael Lynch has drawn attention to the need to look at "where the action is", at the setting where actors and heterogeneous resources are organized spatially and temporally in order to produce objects recognizable as scientific objects. Activities and objects are constitutively linked to modes of organizing a "space of operations" linking human actors, physical locations, instruments and materials in terms of a "grammar of spatial concepts" generating "topical contextures" - "local orderings of referential details exhibiting visible relations of above/below, next to/separate from, inside/outside, before/behind, aligned with/askew, an so on" (Lynch, 1995: 229). Lynch focuses on the settings where actors, technologies, materials and skills meet to generate objects and images, but his approach can be extended to settings involved in the generation of interscalar objects - for instance, through the transformation of texts or inscriptions produced locally into objects capable of circulating translocally in the form of publications, kits or standardized packages of theory/methods or digitalized information. The focus on topical contextures suggests interesting links with the operation of *projection* involved in map-making.

Scientific work generates representations or inscriptions, which are produced through a set of operations transforming "raw" materials - which may consist of three-dimensional objects or of other inscriptions - into texts, figures, tables, graphs or illustrations suitable for specific purposes (publication, public presentation, teaching, circulation among researchers, incorporation into data bases, etc.). These operations include the *filtering* of the elements to be included in

the inscription, the *uniformization* of representational conventions, the *enhancing* of certain features and the *definition* (through the addition of captions or of scales) of what the representation is meant to "show" (Lynch, 1990: 160-66). The similarity with the operation of *symbolization* in cartography comes to mind, here.

These similarities between a cartographic approach and current approaches in science studies call for a more specific justification for its use. They are not alternative modes of research, but rather different ways of exploring and mapping the same territories. On the one hand, the language of cartography is particularly useful when dealing with research themes for which *scale* is a central feature. On the other hand, it allows translations between definitions of research objects, the organization and the geopolitics of cancer research, while, at the same time, focusing on the scale-dependent specificities of objects, approaches and processes.

## 2. Oncobiological research and the "molecularization" of cancer: a view from the semiperiphery[6]

In Portugal, as in other countries, research on the biology of cancer has involved scientists from different disciplines and interdisciplinary fields in the biomedical and biological sciences, including hematologists, immunologists, pathologists, biologists and biochemists, among others. Over the last three years, I have conducted ethnographic research at one of the most important units pursuing research on oncobiology, the Centre for Research in Biopathology and Oncobiology/Institute for Pathology and Molecular Immunology of the University of

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[6]For a discussion of the concept of semiperiphery - first proposed by Immanuel Wallerstein as part of his world-system approach - and the characterization of Portugal as a semiperipheral society, see the contributions to Santos (ed.), 1993. Bastos (1996) offers an approach to AIDS and the global-local links in the production of science which uses a closely related framework.

Oporto (CIBO/IPATIMUP) - which I shall call "the Institute" from here on. The Institute is an independent, non-profit research centre affiliated with "the University of Oporto[7]. The senior generation of scientists at the Institute, most of them in their early to mid-40's, includes a significant proportion of MD's with PhD's in pathology. They have played a prominent role in shaping a "style"[8] of research centered on a complex, multi-scale understanding of cancer. Researchers, technicians and students have often pointed out in conversations that this particular style is a response to the constraints related to the scarcity of skilled scientists and technicians in Portugal, which has forced the Institute to optimize available human resources by diversifying their skills. On the other hand, the small scale of research in this field when compared with that in core countries is an obstacle to organizing the Institute along what some researchers and students call the "assembly-line" model they have seen at work in Scandinavia, the Netherlands, Britain or the United States, and which requires greater specialization and a more rigid division of labour. Even if these are plausible explanations for the peculiar research environment and training schedules prevailing at the Institute, their outcome has significant consequences for its overall scientific orientation and outlook, which go well beyond the responses to "operational" and organizational constraints.

The Institute has strong and persistent links with researchers and institutions in several countries of Europe, Latin America, Africa and the United States, through visiting professorships, participation in scientific meetings and editorial boards of scientific journals, refereeing, joint research projects, training courses in Portugal, the exchange of graduate students and, more generally, through a regular

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[7]For detailed discussions of CIBO/IPATIMUP, of its organization, composition, activities, research programs and output, see Nunes, 1996a, b, c, d. IPATIMUP 1994 and 1997 offer a wealth of useful information on the unit and on its history.

[8]My use of "style", here, is very close to Fleck's (1979) notion of a cognitive style in science, but I have tried to expand it to include all the dimensions associated with scientific activity, like work routines, local adaptations of techniques, articulations of disciplinary or specialty approaches, interfaces between medical and biological concerns or patterns of transnational cooperation.

involvement in what I called elsewhere multisite lab work (Nunes, 1996c). Most scientists at the Institute spent periods of training, as graduate students, in Norway, Sweden and Denmark, which have helped forge a particularly strong "Scandinavian" link, influencing the overall research environment and research orientations of the Institute - this influence is not alien, for instance, to the commitment to research relevant to medical oncology and to the sustained involvement of researchers in the development of diagnostic procedures for cancer. The role of this generation of researchers was central in introducing molecular biological approaches in oncobiological research in Portugal. Over the last two decades, projects based on these approaches or incorporating them in some way have increased significantly, a trend which has been paralleled, since the late 1980s, by the growing enrollment of biologists and biochemists in graduate training and a decrease in graduate students with a background in medicine[9].

**Table 1**

**Background of senior researchers (PhD's) at the Institute, 1996**

| | |
|---|---|
| Medicine | 9 |
| Biology | 6 |
| Veterinary Medicine | 2 |
| Nutrition Science | 1 |
| Engineering | 1 |
| *Total* | *19* |

Source: Elaboration by the author

[9]For a discussion of the relationship between the composition of senior staff, the recruitment patterns of graduate students and the high proportion of women in both groups, see Nunes, 1996c.

**Table 2**

**Background of MA Students (Oncobiology) at the Institute, 1991-96**

| Background | 1991-93 | 1992-94 | 1994-96 | Total 1991-96 |
|---|---|---|---|---|
| Medicine | 1 | 1 | 2 | **4** |
| Biology | 5 | 5 | 10 | **20** |
| Biochemistry | 1 | 1 | 1 | **3** |
| Pharmacy | 1 | 1 | 1 | **3** |
| Vet. Medicine | - | - | 1 | **1** |

Source: IPATIMUP, 1997: 5b-d, 6a-b

**Table 3**

**Background of PhD Students at the Institute, 1994-96**

| Background | Completed | Ongoing | Total |
|---|---|---|---|
| Medicine | 2 | 6 | **8** |
| Biology | 1 | 15 | **16** |
| Biochemistry | - | 1 | **1** |
| Pharmacy | - | 1 | **1** |
| Dental Medicine | - | 1 | **1** |
| Engineering | 1 | 1 | **2** |

Source: IPATIMUP, 1997: 7a-d

The specific "style" established by the generation of pathologists trained in the 1970s and 1980s, however, has persisted, leading to a research environment where the "other" approaches to cancer research which tended to be pushed into the background in other countries - like the United States - still figure prominently and are articulated with molecular approaches based on molecular biology and molecular genetics (Sobrinho-Simões, 1992).

This is clear if one examines the organization of graduate courses in oncobiology, which require students to go through a variety of approaches to cancer research and to develop skills in different types of techniques. These courses extend over three semesters (plus a semester for dissertation work) and

include bi-weekly seminars by guest speakers on specific themes (including the social studies of science!), a "Journal Club" meeting every week for discussion of published papers of interest to researchers and students, allowing them to keep up with updated scientific information, weekly meetings with supervisors, a teaching module offering overviews of subjects, techniques and research areas, and "practical" modules (taught by researchers and technicians), whose aim is to introduce the students to a variety of techniques. A range of optional activities is also offered providing links with other areas of biology and with anatomo-pathological work in medicine. Students are thus encouraged to develop a range of skills which, as mentioned earlier, they themselves often contrast with the highly specialized, "assembly-line" model of laboratory work found in other countries. This training is crucial for the reproduction of the scientific style prevalent at the Institute. It provides a counterweight to the hegemony of the molecular approach, generating a more varied and complex scientific environment and more versatile scientists with a variety of flexible skills. The following tables summarize the subjects included in the two types of teaching modules for the 1994/95 course.

**Table 4**

**Graduate course in Oncobiology, 1994/95**

**Subjects taught in "overview" module**

- Stomach cancer. From pathology to biopathology (I and II)
- Cytogenetics and *in situ* hybridization in oncology
- Experimental models in oncobiology
- Nutrition, food toxicity and cancer
- Breast cancer and the prospects for cytopathology
- Cytogenetics and molecular genetics of stomach cancer
- Hemato-oncology
- Lymphoid biology and oncology
- Epidemiology and etiopathohgenesis of cancer disorders
- Thyroid hyperplasias and neoplasias. A multidisciplinary approach
- Biochemical genetics and population genetics
- Cancer registers and survival studies
- Introduction to immunocytochemical techniques at the optical and ultrastructural levels
- Introduction to techniques of in situ hybridization and molecular genetics
- Causal inference and other questions
- Cancer of the bone and of soft parts as paradigms for sarcomas
- Introduction to techniques of cytometry and dosing of hormone receptors

Source: Graduate Course in Oncobiology (3rd edition), syllabus

**Table 5**

**Graduate course in Oncobiology**

**Practical modules**

Cytology/histology (inclusion, cutting, routine and special staining, basic photography)

Electronic microscopy

Immunocytochemistry, optical and ultrastructural levels (includes immunofluorescence and double marking techniques)

In situ hybridization of nucleic acids and chromosomes in interphase

Molecular genetics

Manipulation of animals for experiments

Flow and image cytometry

Source: Graduate Course in Oncobiology (3rd edition), syllabus

## 3. Mucins, genes and environment: on the uses of molecular biology

The diversity of approaches found at the Institute coexists with a focus on specific types of cancer. Among these, gastric carcinoma figures prominently - along with thyroid and breast cancer. Its high profile in oncobiological research is justified by its very high incidence in Portugal - the highest within the European Union -, making it one of the most important causes of death from cancer in the country. But it also raises several important issues concerning the choice of the

adequate combination of approaches to the study of cancers in which the relative contribution of genetic and environmental factors and their interplay is still largely ignored:

> Gastric carcinoma is a major cause of cancer death worldwide and, like most human cancers, probably develops after environmental insults acting on normal individuals and/or individuals with increased genetic susceptibility. The relative contribution of environmental exposure and genetics for the risk of developing gastric carcinoma is far from being established. Diet and infections, with particular emphasis on *Helicobacter pylori* infection, have been identified as exposure risk factors. In contrast to most Western countries, the mortality rates from gastric carcinoma have not declined in Portugal raising the possibility that the Portuguese population may have some particular genetic susceptibility for gastric carcinoma development (Carvalho *et al*, 1997: 107).

Although genetic factors have been identified and studied which are active in the initiation and progression of gastric carcinoma, this is a type of cancer strongly linked to exposure to environmental influences, namely diet and chemicals used on food. A further and important influence which is particularly relevant for Portugal is the endemic infection of over 80% of the Portuguese population with a bacterium, *Helycobacter Pylori*, which increases the individual susceptibility to stomach diseases and, in particular, to gastric carcinoma. Research on gastric carcinoma thus requires a diversity of approaches which have to take into account the particular relationship between genetic and environmental factors in the susceptibility to the disease and in its initiation and progression. The use of molecular genetic approaches in the study of gastric carcinomas thus displays some interesting features which provide a "point of entry" into the specific "style" of scientific work found at the Institute, and in particular, into the way molecular

biology "fits" within this style. But it also provides interesting information on how the use of molecular genetics in the study of a "peripheral" type of cancer may be intrumental in generating links to the transnational world of molecular biological research.

In 1996, out of fifteen ongoing research projects at the Institute, six focused on gastric cancer or on closely related issues. Among these, two were specifically directed towards the search for new genes in gastric cells and one dealt with the interplay of genetic susceptibility and infection by *Helicobacter pylori* and its role in exposure to gastric cancer. An interesting common feature of these projects was their interest in mucins and in their role in the protection from, and differential susceptibility to, gastric carcinoma.

Previous research, following a "classical" molecular genetic approach to gene mutations during carcinogenesis had shown that "[m]ucin glycoproteins suffer systematic alteration during carcinogenesis in general and gastric carcinogenesis in particular", and that high polymorphism of mucin genes was linked to susceptibility to gastric carcinoma, particularly among "individuals with MUC1 and MUC6 genotypes containing a low number of tandem repeats - coding for `small´ mucins" (IPATIMUP, 1995). Following from the recognition of the role of mucins as "key molecules in gastric carcinogenesis", research was extended in two directions. The first aimed at identifying new mucin genes expressed in gastric cells, since only a small part of them are known. The second direction focused on the role of mucins in the interplay of genetic and environmental factors associated with susceptibility to gastric carcinoma.

A project meant to explore the first direction was launched in 1995, directed by a pathologist with a PhD in Medicine. The research proposal presented it as a

project in the field of the molecular biology of cancer. It involved the "characterization of gene expression (with emphasis on mucin genes) in gastric cancer cells by using an expressed sequence tags (EST's) library".

The actual work involved the completion of several steps. Each of these steps required the use of a set of techniques which have become standard in the field of molecular biology, as well as immunohistochemical procedures, which were needed to evaluate mucin expression with the use of antibodies.

The first step consisted of the "selection of two appropriate gastric cancer cell lines for the construction of cDNA libraries". Both commercial cell lines and lines established at the Institute using samples from patients undergoing surgery at the local University hospital were used and studied. Researchers drew on a variety of techniques ranging from immunohistochemical evaluation of mucin expression using particular antibodies to searching for expression using cDNA probes for the genes of interest in Northern blotting studies and for gene polymorphism in Southern blotting studies. From these gastric cell lines, cDNA libraries were constructed. A commercial fibroblast library was used to remove the sequences shared with the gastric cell lines, in order to "[enhance] the number of gastric specific clones". The next step involved the single direction sequencing with a vector primer of a random sample of about 1,000 "subtracted" cDNA clones. The sequences thus obtained were then compared with information available in gene bank databases, in order to identify known and unknown genes. At this stage, interaction with other research groups working on similar problems and exchange of information was crucial. New genes expressed in the gastric mucin could thus be identified.

A parallel line of research (involving the full-time work of a graduate student) aimed at obtaining monoclonal antibodies to gastric mucins through the

"[p]urification and deglycolisation of gastric mucins from normal mucosas and carcinomas and immunization of Balb/c mice" (IPATIMUP, 1995). An antibody was produced and an attempt was made to negotiate its commercial development with a biotechnology company.

This project rested upon the use of standard tools of molecular biology and upon the creation of links to current work on mapping and sequencing the human genome. It focused on a given scale - the molecular - and, despite its relevance for the development of diagnostic tools for gastric cancer, followed a strategy of standardization and deterritorialization/disembodiment of the phenomena under study. Interscalar links were provided by the parallel work of developing monoclonal antibodies for gastric mucins. But the overall direction of work involved the generation of links with the mainstream of molecular biological research, a process of "downscaling" the object "cancer" to its molecular level. "Downscaling" the object and the approach was crucial in forging a more effective link to global science worlds, overcoming the limitations imposed by the "local" and "peripheral" status of gastric cancer, and eliminating the "disturbing" influence of factors associated with organisms which stand in the way of the standardization of genetic information (Fujimura and Fortun, 1996).

This does not mean, however, that the influence of "local" and "embodied" constraints was irrelevant or negligible. Following the actual work involved in this project showed how these constraints were experienced at different steps. A particularly striking instance of "trouble" emerged at the early stages of the project. RNA had to be obtained in order to produce the cDNA needed for the research. The research proposal specified that cell lines for the extraction of RNA would be of two kinds. One would be commercial, purchased from a biotechnology company, and the other would be created at the Institute. One of the reasons for this was that

some of the relevant variables that had to be controlled if new mucins expressed in gastric cells were to be identified were ignored by biotechnology companies when establishing commercial cell lines designed for a variety of purposes and research interests. Another reason was related to costs: extracting and processing RNA locally was considerably less expensive than buying it. Researchers had to collect tissue samples from operating rooms - which required access to the setting, sometimes difficult negotiations to create a relation of trust with a surgeon, and an uncertain period of waiting for suitable patients with the proper characteristics to show up. The processing of RNA itself was a difficult job, due to the sensitivity of the material, the work was punctuated by difficulties in performing Northern blotting, and the amounts of "usable"RNA were too small for the needs of the project. The research team finally decided to use different types of RNA - commercial and "local" - for different purposes and phases of the work, even if, in principle, "local" RNA, obtained and processed under conditions controlled by the team and based on a detailed knowledge of the relevant aspects of the clinical history of the surgery patients providing the tissue samples, should have been used. In this case, the recalcitrance of materials, the uncertainties associated with the collection of biological samples and the local contingencies of work conspired to force the research team to use standardized materials more extensively than expected[10].

The second direction of work focuses on the role and importance of a particular type of molecules - mucins - in the mediation between environmental and genetic factors. As stated in the introduction to a published paper,

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[10]A more detailed discussion of this episode can be found in Nunes, 1996b. Problems related to local contingencies and adaptations in the use of techniques and to the "resistance" and appropriateness of biological materials are commonly found across the life and biomedical sciences; see the contributions to Clarke and Fujimura (eds.), 1992. Cases involving molecular biological techniques are discussed in Jordan and Lynch, 1992, 1993, forthcoming.

> [m]ucins are attractive molecules to study the relationship between genetics and environment because they play an important role in the protection of gastric mucosa and exhibit a highly polymorphic genetic variation in their length. In fact, mucins are the major structural components of the mucus viscous gel covering the gastric mucosa, and represent the first line defence barrier against environmental aggressions. All mucins have in common the presence of extended arrays of tandemly repeated peptides rich in serine and threonine residues that are potential O-glycolisation sites. The variable number of tandem repeats accounts for the extensive polymorphism observed at DNA, RNA and protein levels. MUC1 and MUC2 are the only two fully sequenced human mucin genes. Several other human mucin genes have been cloned and partially sequenced. The protein product of the MUC1 gene (mammary/pancreatic mucin) has a molecular weight that correlates to the size of the mRNA and to the size of the DNA restriction fragments, suggesting an important gene effect on the final structure of the mucin. All known mucins are secreted products except MUC1 which has a transmembrane anchorage domain leading to a membrane-bound mucin (Carvalho *et al*, 1997: 107).

The high expression of MUC1 mucin on the gastric mucosa led researchers to hypothesize an influence of MUC1 polymorphism on the differential susceptibility of individuals to environmental aggressions leading to gastric carcinomas. Smaller mucins would thus be linked to a smaller protective effect. The testing of this hypothesis rested upon a study based on Southern blot analysis of biological samples from a group of patients with gastric carcinoma and from a control group of blood donors, all Caucasian and living in Northern Portugal. Southern blotting allowed MUC1 gene polymorphism to be evaluated in both groups, showing that smaller mucins tend to be indeed associated with greater incidence of gastric carcinoma.

The very title of the paper reporting on this work, "MUC1 gene polymorphism and gastric cancer - an epidemiological study" articulates two approaches based on different sets of procedures and on ways of constructing the object "cancer" which not only locate this object at different scales, but require that the work of disembodiment and deterritorialization of cancer associated with the genetic approach be related, in some way, to the task of specifying the set of embodied and territorialized "latourian" actors (Latour, 1987) which are part of the standard procedures of epidemiological research - the case-control method, in this instance. These actors include Portugal and the Western countries, genes like MUC 1, bacteria like *Helicobacter pylori*, alleles, molecules like RNA, DNA and mucins, patients with gastric carcinoma and blood donors, techniques like Southern blotting and PCR, VNTR's and polymorphic gene expression... The list could be extended, but it will be enough, for our purposes, to contrast it with a similar list drawn from texts focusing on gene mutation in gastric cancer or on the identification and sequencing of mucin genes. The play of scales and the heterogeneity of the actors explicitly mentioned is different in each of these cases. All of them require some definition of the appropriate scale - or scales - at which the phenomenon of interest is to be identified and research procedures are to be carried out. Most approaches in oncobiology require transformations of biological materials - tissues, in this case - which are irreversible. In other words, materials processed for molecular biological studies cannot be "brought back" to a condition appropriate to immunochemical procedures. The reverse is also true: once submitted to staining procedures, a fragment of tissue cannot be used for molecular biological analyses. The specification of the relevant "topical contexture" of each of these approaches is, thus, closely linked to the scale at which research objects are defined[11].

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[11]This means that, unlike what happens in microscopy, shifting scales is not identical with changing magnification. It actually involves the processing of materials in order to construct objects which are

Articulating apparently incommensurable research objects, constructed through different approaches, thus requires the emergence of suitable topical contextures which are no longer scale-specific, but allow for the interplay of objects and approaches at different scales. How can this be accomplished?

In the work discussed above, different definitions of cancer and of the susceptibility to cancer arising from different approaches are articulated through the production of textual and graphic representations which generate a two-dimensional space where the molecules emerging from work in molecular biology and the organism/environment interface dealt with by epidemiology are turned into elements of tables and graphs through the mediation of the concept of gene polymorphism and of a specific type of protein, mucins. The textual space itself provides a "trading zone" (Galison, 1996) where these boundary objects (Star and Griesemer, 1989; Fujimura, 1992) are transformed into actors in a new story, which articulates the disembodied and deterritorialized objects generated by molecular biology with the embodied and territorialized patients suffering from gastric cancer and the "healthy", voluntary blood donors of the control group.

These instances of research on mucins seem to be appropriate illustrations of different ways in which molecular biological approaches are used at the Institute:

- in the first case, molecular biology is part of a "classical" procedure of identification of genetic mutations associated with the initiation and progression of cancers - in this case gastric carcinomas;

- in the second case, molecular biology provides a link to mainstream work on the mapping and sequencing of specific genes - in this case mucin genes -, as a

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scale-specific.

contribution to the human genome project[12];

- the third case, finally, articulates a "contextual" or "multiscale" approach to the study of the role of genetic polymorphism - in this case of mucins expressed in the gastric mucosa - in providing differential susceptibility to gastric carcinoma, as part of a more general study of the specificity of gastric carcinoma in Portugal. A combination of epidemiological and molecular approaches and languages is articulated in textual and iconographic form.

## 4. Conclusion

Research on stomach cancer and, more specifically, on mucins highlights an interesting relationship between representations of cancer as a scientific object, of the organization of cancer research and of its different orientations and of the geopolitics of cancer research. A common theme linking these three sets of representations is that of the interplay of scales involved in each of them. The language of cartography may be a powerful tool for making sense of this interplay. As a step in the project of drawing a cartography of cancer research, this paper tried to bring into focus some relevant issues which tend to be invisible in studies focusing on core settings in the transnational worlds of science, by providing a partial, situated view from the semiperiphery. It may be useful to conclude with a brief comment on what appear to be the most significant outcomes of this exercise, focusing on the role of molecular biology in cancer research in the particular setting dealt with here.

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[12] I use the expression "human genome project" in the wide and loose sense proposed by Fujimura and Fortun (1996: 161): "an ongoing effort since the late 1970s involving many scientists, public institutions, private corporations, and national governments to fund and carry out the research of mapping and sequencing human genes, and to develop the basic tools and materials of recombinant DNA research".

Molecular biology provides important tools allowing locally relevant work to be translated into global, mainstream research. This was accomplished, in the cases mentioned, through the definition and manipulation of a specific research object, mucins, which played the role of boundary objects in the interplay of scientific approaches and scales. Research focusing on the molecular scale made it easier to generate disembodied and deterritorialized, standardized, transportable knowledge, allowing researchers to participate in transnational science worlds and to have their research recognized as globally relevant. Articulating molecular biology and epidemiological approaches by focusing on the role of mucins in protection against environmental aggressions, in turn, allowed the potentially reductionist bias associated with the first approach to be balanced by a sensitivity to the embodied and contextualized interplay of different factors at the origin of the susceptibility to a "local" and "peripheral" type of cancer. This raises interesting questions concerning the ways in which "paradigm shifts" may be articulated through the emergence of new configurations of "old" approaches.

It remains to be seen whether the territory of oncobiology will be able to expand and explore the relational and multiscale approach beyond factors conventionally defined in the field as "environmental", towards an incorporation of conditions usually described as "social", "cultural" or "political", still regarded as outside its proper field of study.

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