DNA Repair 12 (2013) 466–471

Contents lists available at SciVerse ScienceDirect

DNA Repair

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

Historical reflections

DNA Repair: A changing geography? (1964–2008)

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ARTICLE INFO

Article history:
Received 26 November 2012
Received in revised form 11 April 2013
Accepted 11 April 2013
Available online 11 May 2013

Keywords:
Spatial scientometrics
Geography of science
Scientific community
DNA Repair
Nucleotide Excision Repair

ABSTRACT

This article aims to explain the current state of DNA Repair studies' global geography by focusing on the genesis of the community. Bibliometric data is used to localize scientific activities related to DNA Repair at the city level. The keyword "DNA Repair" was introduced first by American scientists. It started to spread after 1964 that is to say, after P. Howard-Flanders (Yale University), P. Hanawalt (Stanford University) and R. Setlow (Oak Ridge Laboratories) found evidence for Excision Repair mechanisms. It was the first stage in the emergence of an autonomous scientific community. In this article, we will try to assess to what extent the geo-history of this scientific field is determinant in understanding its current geography. In order to do so, we will localize the places where the first "DNA Repair" publications were signed fifty years ago and the following spatial diffusion process, which led to the current geography of the field. Then, we will focus on the evolution of the research activity of "early entrants" in relation to the activity of "latecomers". This article is an opportunity to share with DNA Repair scientists some research results of a dynamic field in Science studies: spatial scientometrics.

1. Introduction

DNA Repair studies are now around fifty years old. Yet, pioneers have not forgotten that "not too long ago, DNA Repair was considered an odd little corner of biology, largely studied in a rather oblique manner by radiobiologists" [1]. One of the main reasons for this marginality is geographical. At the beginning, DNA Repair scientists were found in different centers than classic molecular centers such as Caltech or Cambridge University [2]. After the Second World War, radiobiologists were asked to study the effect of radiations on human cells and, for this matter they were often located in nuclear research centers and cancer research centers. Step by step, the "DNA Repair field" broke off from radiobiology to become its own critical branch of biomedical research. The introduction of the keyword "DNA Repair" in 1964 and its rapid spread throughout the world can be seen as the birth of the DNA Repair community [3–5]. Between 1965 and 1975, 2000 authors mentioned "DNA Repair" in the titles of their articles hailing from almost 200 different urban areas and from at least 32 different countries. Such a rapid diffusion of the keyword throughout the scientific world suggests the DNA Repair field did not grow out of a void. As suggested by Errol C. Friedberg, before 1964 future DNA Repair scientists were already attending radiobiology or photobiology events together as well as more generic events regarding biology [6].

In the historical reflections published thus far in the journal *DNA Repair*, it appears that the evolution of the scientific field has a lot to do with individuals' careers. Of course, the geography of scientific activities is strongly related to scientists' opportunities of mobility and collaborations. Yet, such opportunities are not independent of the social, economic and political context in which scientists are involved. Thus, while Moscow was the second top publishing place in the field after the San Francisco Bay Area between 1965 and 1975, it fell after the top 100 nowadays, obviously a consequence of the general decline of Russian science after the USSR collapsed. On the contrary, Seoul and Beijing, which were not active at the beginning of the field, are now among the top publishing places in DNA Repair studies. Those evolutions show how much scientific activities are connected to society and economic issues.

In comparing the location of the "DNA Repair" papers published during two times periods (1965–1975 and 2006–2008) from 30 years out, we will try to show the spatial spread of the DNA Repair community and its evolution over time, insisting on the influence of the past over the present situation.

1.1. The social study of science

In Science studies, bibliometric data used to analyze the structure and the dynamics of a scientific community is a well-known

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http://dx.doi.org/10.1016/j.dnarep.2013.04.002

approach [7]. Progressively, social scientists tend to pay more attention to the location of scientific activities [8]. Along this line, in this article we seek to use bibliometric data extracted from both Scopus and the Web of Science (WoS) for geographical purposes by using the addresses of the authors.

Publication practices have changed after the nineties with higher incentives to publish and collaborate, the development of Information and Communications technologies (ICTs) and the growth (in total number of scientists) of the global scientific community. Beyond the changes in the publication practices, the major difference between the 1965–1975 period and today (2006–2008) for the DNA Repair field is the evolution from an "emergence stage" toward a "mature stage" of the research question. In studying the history of the famous "phage group", in the 70s, the sociologist Nicholas Mullins showed how scientific practices change when moving from a stage of research to another [9]. Contacts between scientists tend to intensify until the community reaches a stable stage. At the same time, scientific problems tend to grow more complex, justifying a higher level of collaborative efforts.

As far as DNA Repair is concerned, some specific features have to be mentioned: right away, different branches developed which were investigating different repair mechanisms. The diversity of the organisms, the diseases under scrutiny and the different chemical nature of DNA damage explain that we can now distinguish many sub-groups inside the community. Moreover, after the nineties, some DNA Repair groups began to interact more and more with other molecular biology groups such as, in the case of Nucleotide Excision Repair, transcription scientists. In spite of this complex configuration, field pioneers have contributed to the preservation, cohesion and the autonomy of the community. The community has its own journal (*DNA Repair*) and its own traditional events. Thus, we expect that in using the keyword "DNA Repair" to extract articles from the bibliometric databases, we will have a representative overview of the community and its evolution.

1.2. The data corpus

In order to have a representative picture of the field genesis, we extracted from Scopus all the articles published between 1965 and 1975 containing the keyword "DNA Repair". We used Scopus because, at least in biomedicine, this database is more precise than the WoS for this early period (Fig. 1). The author's addresses are more often indexed than in the WoS, as well as the keywords. However, even in Scopus, the overall data quality for 1965–1975 is lower than it is now. Therefore, when the keywords and the abstract were not indexed, the search was only based on the title of the articles. Collaborations are almost never specified in the database for 1965–1975. Often, there is only one address by paper even if the paper was written by scientists from several places. When, for a given article, no address was specified at all, we used, when available, the address associated to another article of the period written by at least one author in common with this article. This method has its limits since scientists might move from place to place during the period. At last, over 1804 articles have been extracted for this period of time and we were unable to attribute an address for only 129 of them.

To get a picture of the present days, we have chosen to extract, from the Web of Science, the DNA Repair articles published between 2006 and 2008. The Web of Science and Scopus offer comparable results for the present period so that there is no reason to prefer one database over the other (Fig. 1). Considering the changes mentioned before, we expect a three-year period is enough to localize the current actors of the community. 5086 papers have been extracted for 2006–2008, to be compared with the 1804 we could identify for the earlier period.

The scope of spatial aggregation chosen for our set of localized bibliometric data is the urban area. It is distinct from the city scope since it includes suburban areas (for instance, Paris and Villejuif are counted together, as are Bethesda and Washington, DC). In some cases, the high density of population and closeness of places justifies the grouping of important cities together such as in Japan (Kyoto–Osaka–Kobe) or in the Netherlands (Leiden–Rotterdam). The advantage of this level of analysis is that it enables to compare data at global level while maintaining satisfactory spatial accuracy to localize scientific activity.

800 different urban areas were active in 2006–2008, (four times the number of urban areas – 195– active during the emergence stage). From the 195 initial places we could identify, 175 were still active in 2006–2008 and are marked in red on the following map (Fig. 2).

2. The evolution of the DNA Repair geography

The "DNA Repair community" emerged in 3 "core areas": Northern America (USA), Europe (with Israel), and Japan. It has progressively spread all over the world. Research centers are now active on the 5 continents, with characteristic concentration patterns (Fig. 2): the "3 cores", and more recent entrants such as China-Korea, India, the southern part of Latin America, Australia, the Persian Gulf, etc.

2.1. The diffusion process

Nearly all the publishing places identified during the emergence stage are still active nowadays (175 out of 195). From the remaining "pioneer cities", sixty are in the United-States and the rest of them mainly in Western Europe (in particular Germany, the United Kingdom, Italy, the Netherlands, and France); Japan and Canada. They were, with Russian cities, the most publishing places between 1965 and 1975. Considering the map, we can draw two observations. We already pointed out the fact that the DNA Repair community has spread globally and developed in countries which were absent at the beginning. However, we can also observe that the diffusion process took place, for the most part, in the vicinity of the "pioneer cities". Both observations are correct since 77% of the "new" localities belong to countries which were already publishing during the first period. At the same time, eleven "new" countries register more than four active localities: China, South Korea, Mexico, Portugal, Taiwan, Argentina, Ireland, Iran, South Africa, Thailand and Tunisia. China has registered the most dramatic evolution, recently entering the field in the eighties and now hosting 40 active places. Only two countries have more localities involved: Italy (43) and the United-States (126). Coming after, Spain, France, Brazil and Japan are the countries where the diffusion process has been the most intensive. This spatial diffusion process is natural considering the maturity of the DNA Repair field. Due to its relation to important health issues (cancer and aging) the field has grown as a key area. However, it is usually perceived to be more difficult and costly to specialize in a field long after its emergence. It is possible to consider this process as a race: those who start in late will have trouble catching up with the others. If it is truly the case, the latecomers would not contribute as much as the early entrants to the total production. The geographical approach offers an opportunity to question this hypothesis at different levels.

2.2. The deconcentration of the production

Between 2006 and 2008, the papers were less concentrated in the main scientific centers than during the emergence period. In 1965–1975, 40% of the production originated from the top ten cities

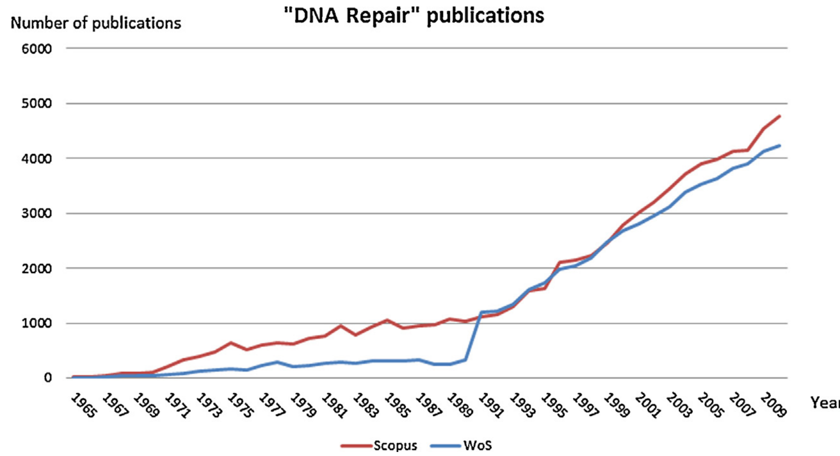

Fig. 1. The "DNA Repair" publications registered in Scopus and the Web of Science. The number of "DNA Repair" publications per year registered in Scopus is higher before the nineties. A "DNA Repair" publication is a publication where "DNA Repair" is specified either in its title or its abstract or its keywords.

while in 2006–2008 the top ten cities represented only 23% of the entire production (5086 articles).

The figures used in this analysis are based on fractional counts. It means that an article signed by researchers from two different urban areas accounts for 0.5 for each city, while it accounts for 1 if signed only by authors working in the same urban area. Thus, adding the contributions of each urban area gives us the total number of articles written during a given period. It would be risky to directly compare the figures for the two time periods, for two reasons. Collaborations and co-authorships were much less developed in the sixties than now; and, in the databases, collaborations were not correctly indexed in the first period. A direct comparison of publications figures in a given city makes hardly sense. In our analysis we preferred to use trends and dispersion/concentration indexes to assess evolution.

A brief look at the recent production map (Fig. 3) suggests that, as we suspected, there are 'pioneer' urban areas which were contributing a lot to the DNA Repair production between 2006 and 2008. Indeed, taking them all together, the 175 'pioneer' areas are accounted for 65% of the 2006–2008 production (3304 articles). The major actors of the field's current dynamic are among them. However, they appear to not necessarily be those one could have expected based on the 1965–1975 production (Fig. 4a and b).

While the San Francisco Bay Area hosted a concentration of 9% of the production during 1965–1975 (143 articles, rank 1), it published 1.5% of the 2006–2008 production (84 articles, rank 11). The New-York agglomeration, the third publisher in 1965–1975, became the first publisher in 2006–2008 (with 166 articles, 3% of the total 2006–2008 production). Contrary to those areas which have stayed ahead in the DNA Repair race until today, Moscow (Russia) and Knoxville TN (including Oak Ridge laboratories) which were respectively the second and the third (*ex aequo* with New-York: 68 articles) publishers during the emergence period (both publishing more than 4% of the total 1965–1975 production) have contributed to less than 1% of the 2006–2008 total production (Fig. 4a and b). Those cases are the most extreme cases of decline

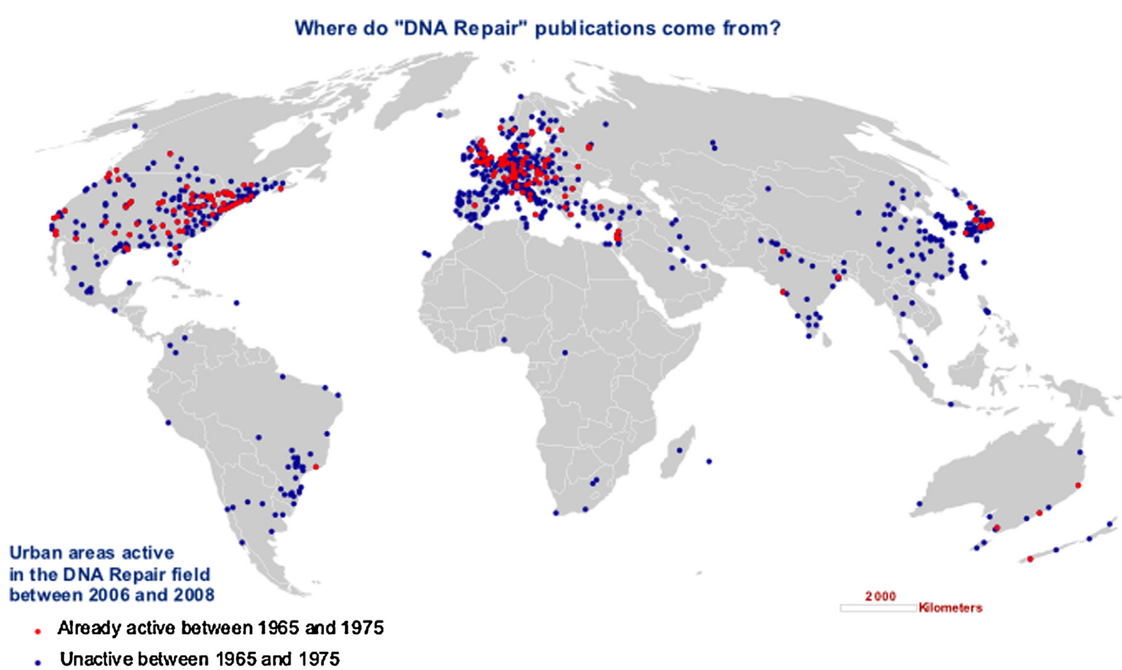

Fig. 2. The geographical diffusion of the "DNA Repair" community. Each point is an urban area where DNA Repair publications have been published between 2006 and 2008. The diffusion happens for a big part in the vicinity of pioneers' areas.

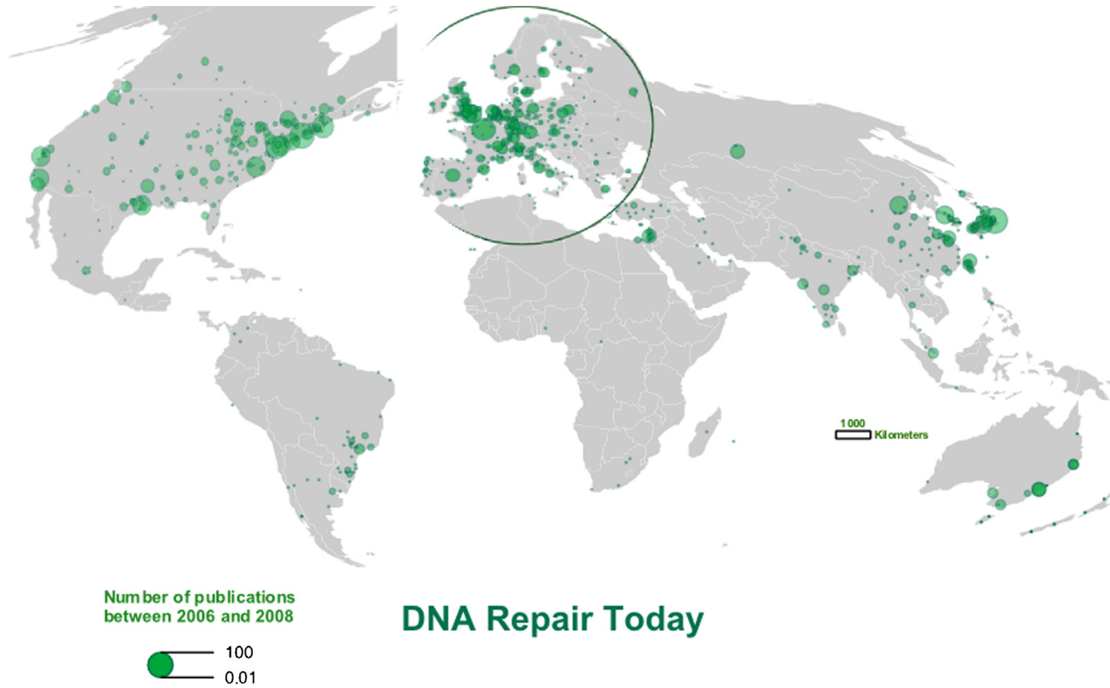

Fig. 3. The locations of the "DNA Repair" publications published between 2006 and 2008. The figure shows the amount of publications per cities which has been published between 2006 and 2008.

in our corpus of analysis; focusing on them, two major factors of decline for DNA Repair teams can be highlighted.

3. Evolution profiles

3.1. The declining centers

As far as the Oak Ridge National Laboratory is concerned, the decline is due to reductions and transformations in the biology division following the eighties' budget cut. This division lost 40% of its members at the beginning of the eighties and had to focus on more applied researches [10]. Richard Setlow has left for Upton (Brookhaven laboratory) and later, Sankar Mitra moved from Oak Ridge to The University of Galveston in Texas. Actually, from the seventies, the role of the national institutes of research has been challenged in many states. From this time on, universities are expected to be the place where fundamental research is done. As a result, many of the DNA Repair teams which developed in nuclear research institutes have finally moved out. In Netherlands, the DNA Repair scientists working in the TNO institute in Rijswijk (a unit of the national institute for applied research) at the end of the sixties, partly moved to the newly created cell biology department in Rotterdam University (led from the seventies to the nineties by Dirk Bootsma). For the same reason, among the very few 1965–1975 localities that are no longer publishing on DNA Repair in 2006–2008, there are Chalk River and Pinawa which both are Canadian nuclear research centers. This move, from national institutes of nuclear research to universities, together with the change in the field's identity inside the scientific world are a key factors in understanding the changes in DNA Repair geography.

As far as Moscow is concerned, the decline cannot be separated from the collapse of the USSR. The two major institutes at that time were: the institute of general genetics (USSR Academy of Science) directed by the famous Nikolay Dubinin (one of Lyssenko's major opponent) and the N.F. Gamelaya Institute in Epidemiology and Microbiology (USSR Academy of Medecine) directed by Adelina Skavronskaya. Major changes in the DNA Repair geography as well as in the overall science geography are related to the decline of the Soviet science [11]. Unexpectedly, on the production map, we can see that DNA Repair studies are now very well developed in Novossibirsk. This city was not active during the emergence stage and now Repair scientists are working there. Thus, Novossibirsk is one of the few centers who, in spite of their late arrival, succeeded in specializing in the DNA Repair field (Fig. 4b).

3.2. The new challengers

Pioneer areas are still active in the field, but some of them are much less involved in the field than they used to be. Nevertheless, in 2006–2008, all the localities in the top seventeen happen to be pioneers. Still, some of them were definitely unexpected. The most extreme case is Madrid where only two papers were published in 1965–1975. It was the only Spanish locality during the emergence period. The end of the Franco era and the integration of Spain into the European Union have been critical for the progress of the Spanish science. Thus, as we have seen before, several Spanish localities are now involved in the field. With a total of 115 papers published in 2006–2008, Spain is now part of the top ten publishing countries.

Globally speaking, pioneer countries have succeeded in staying ahead in the race (in part thanks to the intra-national diffusion process), but China has entered the 2006–2008 top ten in Russia's former place. South East Asia's entrance into global science needs to be highlighted since it is in China and South Korea that we have found the most remarkable cases of catching up. Indeed, among the 625 urban areas who were not publishing during the emergence stage, Seoul and Beijing are the only "latecomers" who are in the 2006–2008 top 20. This change is consistent with the evolution of the whole system of international science registered by the WoS [12]. However, Seoul and Beijing are not among the top 20 time-cited areas. Instead, it is Zurich and Oxford. Therefore, even if Seoul and Beijing are producing more than Zurich and Oxford, they are less visible and influential than them at the global level. Contrary to Seoul and Beijing, the 18 other top publishing areas are also part of the top 20 highest cited areas. It shows there can be a certain lag

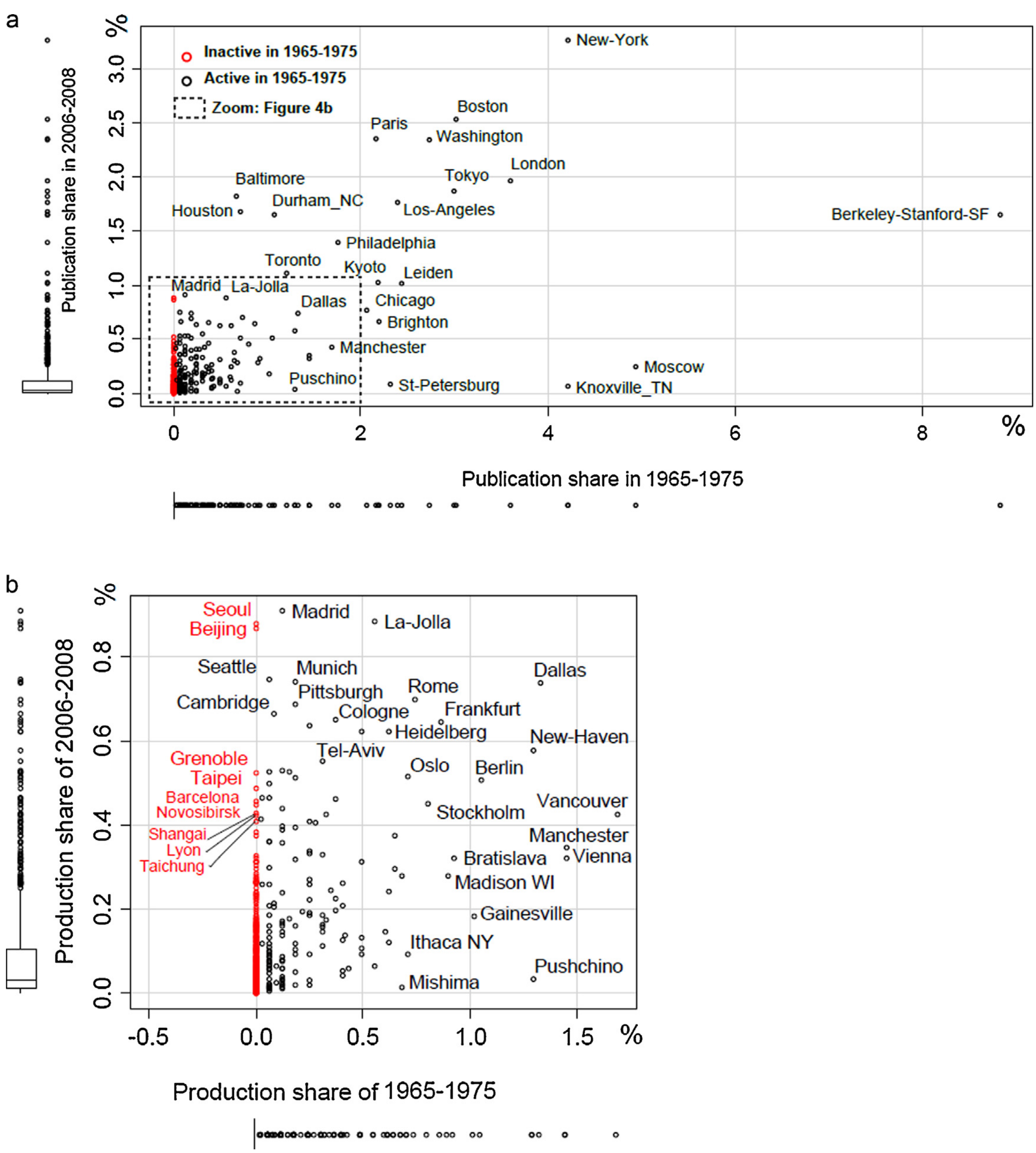

Fig. 4. (a and b) The Evolution of the publication share. How important is the current activity of a given DNA Repair production area compared to its activity during the genesis of the DNA Repair field (1965–1975)? Although 5% of the 1965–1975 "DNA Repair" publications are coming from Moscow, it is only 0.25% of the 2006–2008 "DNA Repair" publications which is produced in Moscow. Although not publishing in 1965–1975, Seoul and Beijing have each produced more than 0.8% of the 2006–2008 "DNA Repair" publications.

between the productivity level and the visibility level of scientific teams. In the case of Seoul and Beijing, the lag is important since Beijing is only the 28th most cited area and Seoul, the 35th.

3.3. *"Catch me if you can"*

The decline of Soviet science and the entrance of South East Asia in the game explain a lot of the changes we can observe. Does that mean that our results are consistent with those obtained by Powell about biotechnology firms: "not all the early entrants turn out to be winners and some latecomers attain prominence" [13]? It could not be the case if we only consider "pioneers cities" located out of the specific contexts of Southern Asia and Russia. Maybe, outside those specific areas, "early entrants" do not enable the entrance of "challenging cities" at the national level. Yet, this does not seem to be the case. "Latecomers" from emergent countries (China or South Korea) are not the only "latecomers" who have been able to attain prominence: Grenoble (France), Barcelona (Spain), Lyon (France), Quebec-city (Canada) and San Antonio (TX, United-States), although inactive during the first period and located in countries already active, have succeeded in becoming part of the highest publishing DNA Repair places in 2006–2008 (more than 20 articles published). Thus, we can observe cases of "catching-up" everywhere that is to say, not only in South Asia.

Even if it has been possible for some late-created teams to become important contributors of the field, it could however have been more difficult to specialize in a specific branch of the field. For instance, the Nucleotide Excision Repair (NER) branch being one of the oldest branches of the DNA Repair field; it might be more difficult or less attractive for a newcomer to become a NER specialist when entering the DNA Repair field "later". To test this hypothesis with our current methodology (we did categorize 50%

			BER	NER	MR	DSB	HR**	Total
Number of "specialized" publications			444	612	255	1080	475	**2404**
Specialized urban areas*	active in 1965-1975 (112)	% of publications	66,69	68,57	74,48	76,63	78,97	**72,51**
	inactive in 1965-1975 (106)	% of publications	33,31	31,43	25,52	23,37	21,03	**27,49**

**Specialized urban areas = Urban areas having produced at least 3 specialized publications in 2006-2008*

***Homologous Recombination is a part of the sub-field named "DSB" (Double Strand Breaks)*

Fig. 5. "DNA Repair" sub-fields and cities' specializations. 112 pioneers' areas (active in 1965–1975) have produced at least 3 specialized publications in 2006–2008 and 106 latecomers' areas (inactive in 1965–1975) have done so. Together those 218 urban areas have published 2404 specialized "DNA Repair" publications. 72.5% of those 2404 publications were produced by the 112 pioneer's areas. However, the 112 pioneer's areas only produced 68.5% of the 612 "Nucleotide Excision Repair" publications. The "Double Strand Break Repair" publications are more often signed by pioneers' areas than the "Nucleotide Excision Repair" publications.

of the 2006–2008 articles according to specific keywords for each sub-field), we have found that among the 41 countries entered after 1990 not a single one published more than 10 "NER" publications in 2006–2008. 18 urban areas are obviously specialized in NER researches (more than 7 articles in 2006–2008). Among them, 15 urban areas are early entrants and 3 of them are latecomers (Barcelona, Strasbourg and Sao Paulo). Actually, this proportion is consistent with the overall proportion of new entrants in the whole "DNA Repair" top 20 (2 latecomers for 18 early entrants). In Strasbourg, the scientific evolution of the NER branch explains its specialization. Indeed, since a link has been found in 1993 between the NER mechanism and the Transcription factor, it has enabled the Strasbourg's transcription team to enter the NER branch. Actually, compared to other sub-field, the specialized latecomers (having published more than 3 "specialized" articles in 2006–2008) are contributing more to the NER and to the Base Excision Repair (BER) publications than they do to others subfields (in particular Double Strand Breaks (DSB) repair mechanisms). Although there are no latecomers in the "Homologous Recombination" (HR) top 20 and in the whole "DSB" top 20, there are 3 latecomers in the "BER" top 20 (Beijing, Novosibirsk and Genoa) and in the "NER" top 20 (mentioned above). Finally, contrary to our initial hypothesis, the level of participation of the latecomers specialized in "excision repair mechanisms" (BER and NER) is higher than expected regarding the global level of participation of latecomers in the sample of specialized articles (Fig. 5). Since it takes time to become specialized in a sub-field and since the study of excision repair mechanisms (BER and NER) was promising in the 90s, we believe new excision repair teams developed at that time, justifying our findings.

4. Conclusion

The major changes in the geography of DNA Repair are the changes which have affected the geography of scientific activities in general. Those changes depend on economical and political evolutions both at a local and a global level. Nevertheless, the internal dynamics of the DNA Repair field are also critical for its development. In order to spread, the field needs to remain attractive for new scientists. The field's clear promise fuels the creation of new active teams in several places in the world. Notably, at the beginning of the nineties the field had succeeded in opening to other areas of molecular biology such as DNA transcription. This evolution has contributed to enhance its diffusion and visibility. In the future, the world's leading active pole of the DNA Repair field must leave their comfort zone to ask the right questions and seek out the required technologies to answer those questions. For instance, the field could find a new breathing space in studying DNA Repair directly in living organisms. For this, new windows of exploration new tools and new technologies are needed. Some of these tools have been already built (Giglia-Mari 2009 Plos Biology [14]) but the effort does not seem to be widely replicated. Another boost in the DNA Repair field could be given by research groups studying the impact and consequences of DNA damage in the epigenetic make-up of the cell. As it grows, the field has become more complex and no scientist can now have a complete overview of this scientific community. Thusly, at this stage, geography can help tracking the dynamics of the field. For instance, we can wonder if there is a need for a better coordination of the field members at the global level. Analyzing scientific collaborations can be a way to assess the level of coordination and measure the cohesion of the field.

Acknowledgments

This work was supported by the Agence Nationale de la Recherche (project GEOSCIENCE, call "Sciences, technologies et savoirs en sociétés"). We are grateful to Drs. M.Grossetti, B. Milard, M. Baron, K. Frenken, L. Jégou for helpful discussion. Thank you to J. Carnine for her helps to check the written English. We would like to thank Drs. D. Bootsma, N.G.J Jaspers, L. Mullenders, P. Lohman,H. Van Steeg and H.T. Riele for kindly sharing with us their DNA Repair story.

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