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A Tale of Two Genome Institutes:
Qualitative Networks, Charismatic Voice, and R&D strategies —
Juxtaposing GIS Biopolis and BGI

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Abstract:

The journalistic stereotypes — of BGI, the world’s largest sequencing center, as a Chinese state venture, and of Singapore’s GIS as a neoliberal platform — are inverted. Methodologically, by looking at qualitative networks, charismatic leaders, and research strategies, this essay proposes a finer grained, meso-level, ethnographic analysis that allows for multi-scalar tracking, and juxtaposition as a generator of comparative insights. It deploys a social hieroglyphic analysis of the leaders of BGI, and an updated account of the post-2010 “industrial re-alignment” of GIS, to highlight the role of cross-national networks in the construction of what are usually seen as national science projects, as well as the roles of mixed state and market strategies, and mixed clinical, basic science, biotech, and big pharma protocols and platforms of the contemporary life sciences. It pays particular attention to the small worlds of the scientific republic and the charismatic voice of leaders forging new institutional arrangements. [149 words]

Keywords: Biopolis, BGI, science cities, qualitative networks, science in Asia, genomics, life sciences

The way that we look at them is very clear: their pedigree, their accomplishment, their energy, and how forward looking they are.

GIS senior administrator on selecting GIS Fellows, April 2015

Introduction

In a previous essay (Fischer, 2013a), I described the unfolding of the first ten years of the Genome Institute of Singapore (GIS), as part of the large Biopolis life sciences enterprise in Singapore, itself part of a series of larger research and development and educational initiatives, directed both at positioning in a global landscape and at creating a new Singaporean grown and staffed knowledge economy. That essay ended with an effort by A*STAR (Agency for Science, Technology and Research), the funding agency, to redirect the institutes from only basic science to more alignment with both industry ('biologics', patents) and clinical science ('translation'). In the present essay, I want to briefly explore how that reorganization has played out amidst a series of subsequent shifts. However, I don't want to just focus on the Singapore story, but attempt to begin a larger comparative discussion of charismatic and institutional growth with a focus on what I will call *qualitative networks*, by juxtaposing the case of another well-known genome institute, BGI in Shenzhen, China.ⁱ I will do so in a slightly different manner than the comparative component in the first essay on the scientific contributions to the stemming of the SARS pandemic and the building of transnational infectious disease monitoring and biosecurity systems at GIS and in Hong Kong.

Traditionalists may balk at the strategy of *juxtaposition* rather than direct *comparison*, but I argue that in the complex world of the life sciences, it can be more productive to engage a set of *mixed methods* in order to begin to characterize the institutional *fields of emergence and competition*. I have called earlier ethnographic forms of this approach a "*mosaic approach*," "*an ethnographic jeweler's eyed detailing of emergent "third spaces"*," "*multi-locale approaches*" (or now more widely called "*multi-sited*" approaches," and attention to the "*peopling of technologies*."ⁱⁱ These

are tools both for globally distributed, *multi-scalar*, and *locally differently grounded* processes, such as the growth of the chemical and nuclear industries and their trailing toxic clean-up imperatives (Fortun, 2001; Petryna, 2001), the pharmaceutical industries and their trailing health care system imperatives (Biehl and Petryna, 2013; Petryna, 2009; Sunder Rajan, 2006, 2012; Waldbly and Cooper 2014), global oncology clinical trial platforms and protocols (Keating and Cambrosio, 2012), climate change science and local vernaculars of appropriation and resistance (Callison 2014), and, here, more generally, the basic life sciences and their translational imperatives. Juxtaposition is a tactic of not abstracting from context (the bane of moving too quickly to generalization and comparative evaluation), while yet being able to gain a perspective on similarities and differences that may open up new ways of doing things in the varied local sites (Marcus and Fischer, 1999).

While I have longer fieldwork experience in Singapore, I have talked to the three founders of BGI, listened to them on several occasions, particularly at five annual meetings of the Human Genome Organization. Again, this is not a comparison of the two Genome Institutes, but rather I want to look more closely at one telling by one of the three founders of BGI, to highlight the role of cross-national networks in the construction of what are usually seen as national science projects. As one listener to the original presentation of this essay (and fellow STS scholar of Asian science) warned, Wang Jian's version of the story is not the only one, and yet she agreed, as long as it is marked as *his* account, it is an important and valid one. And, for my purposes in this essay, it raises for me a series of structural insights and questions, access for further exploration into the global competitive dynamics of the life sciences.ⁱⁱⁱ Methodologically, in one sense, it draws upon the experiments to reinvent or refunction the ethnographic interview that were explored in the 1990s in the eight volumes of the *Late Editions Project*, edited and guided by George E. Marcus, and published by the University of Chicago Press (Marcus, ed., 1993-2000). At issue in those experiments was an informed encounter, *ethnographic* contributions, rather than merely interviews, having to do in part with strategic access points in processes that are not visible or available in conventional accounts

(see those volumes and especially their methodological introductions and conclusions for further elaboration).

In the present case, I am interested in both what I call in the title “qualitative networks,” that is, mentorship and friendship relations that are part of the *small worlds* of the *scientific republic* (a transnational mapping that acknowledges but transcends and often contests political boundaries and national projects), and in what I call the *charismatic voice*. I’ve dealt with the charismatic voice in various ways before, as an interest in the “lively languages” that scientists use (and that often provide metaphors for changes in lay consciousness, as well being a two way street between science and popular culture), the “songs and under-songs,” of science (that is the debates about ethics, ability to foretell abuse and misuse of new developments, or more generally fears and grounds for reassurance), and particularly with capturing the tonalities, nuances, and resonances that scientific leaders use when they are in their most lucid and explanatory moments. I have tried to capture that lucidity and expressiveness explicitly with Dr. Judah Folkman’s account of the angiogenesis inhibitor story for cancer therapy (Fischer, 2010, 2012), and in a slightly different way with discussions of scientists’ autobiographical accounts, as opposed to biographical accounts (1994, 1995, 2003, 2009).

I am less concerned in this piece with variants of founding stories than with drawing attention to forms of network analysis that include mentorships, funding, and political leverage that can help institutions against internal inertial and bureaucratic blockages. One might call this rhizomic networks if one wants a fancy word, but “qualitative” may be simpler and just as good. In part I of this essay, I will, very briefly, bring the account of the Genome Institute of Singapore up to date as it prepares for yet another five year plan for funding. In part II, I present an account of BGI in Shenzhen that may complicate stories that contrast the GIS as driven by transnational “foreign talent” in an effort to create a new Singaporean scientific community, and that see BGI as a state enterprise that can use state backing to underprice services to gain market advantage (e.g. Lauerman, 2012). As Wang Jian points out, much of the stereotyped discourse generated in competitive publicity is not only unfair, but also a source of misrecognition.

I. *Biopolis Reoriented*: the Cell, Translation, Computation, and Institutional Ecologies

My first fieldwork report on Biopolis and GIS chronicled the three areas of scientific advance that put the Genome Institute of Singapore (and its sister biology institutes) on the global map as a scientifically competitive basic science research center: first, infectious diseases with the role of GIS in the SARS crisis; second, “scientific diplomacy” in moving the office of the Human Genome Organization to GIS and using a molecular anthropology research project to begin establishing working relationships between richer and poorer scientific communities in the Pan-Asian region, the Pan-Asian SNPs Consortium; and third, the productivity of papers in the realm of iPS stem cell research, cancer, and tissue repair.

That paper (Fischer 2013a) ended chronologically with the aftermaths, short-term anxiety, and shifts, that followed the October 2010 decision to ‘industrially align’ the seven basic biology research institutes of Biopolis. This decision came suddenly, like a Friday decision in the business world (viz. Judah Folkman in Fischer, 2010, 2012). Not only did the charismatic founding director of the Genome Institute leave Singapore for a parallel effort in the U.S., followed by several key P.I.s (principal investigators), but there ensued two years of anxiety and downsizing as budgets were withheld and mortgaged. More P.I.s were let go because their direction of research no longer fit with the projected directions of the Institute. A couple of younger scientists were promoted to senior P.I. status. Two intense years followed of writing many grant applications, of working out contracts with the commercial biotechnology and pharmaceutical worlds, and working out collaborations with the clinician community (especially in eye diseases, and lung cancer research).

More generally, it was a time when there seemed to be a more general move in national and transnational research agendas towards the cell as increasingly available as a unit of study, rather than the twentieth century focus on the gene, and thus towards epigenomics, developmental biology, cell reprogramming; and commercially towards biologics or cell based production of medications rather than chemical pharmacology.

GIS emerged by the turn of 2015 with a new set of networks, pipelines, and collaborations -- with clinicians in cancer research at several hospitals, research and licensing collaborations with biotech companies such Fluidigm and Singapore based SG Microlab Devices and with a couple of hopeful start-ups. Today preparations are under way for a new five year cycle of funding, 2015-2020, and with a number of new players in the game in Singapore. Not only has money been shifting to the now world-ranked research universities, scholarships for non-Singaporeans are being reduced, and Merck has come to try to engage more fully with the Singapore research community by hiring a member of GIS as its point person for identifying scientists and projects with whom it might collaborate, attempting to bring together the resources and ways of moving projects through the pipeline of big pharma with the cutting edge insights in more nimble upstream research groups.

GIS sees itself now as a mature and stable Institute, with a process of continual renewal, having promotional positions parallel to university ranks of assistant professor (senior research scientist), associate professor (group leader) and full professor (senior group leader) as well as Fellows (returnees from A*STAR's ambitious program of scholarships for training at the BSc, PhD, and postdoc level in leading universities and laboratories abroad). As new investigators are hired at all levels, the focus of the Institute shifts with their interests, grants, and strategies.

Transition Period 2011-2015: Cell, Epigenetics, Reprogramming

'Friday decisions' happen more often in business than in academia or national research labs, and are often assessed in terms of pure returns on investment, efficiency and flexibility in conducting mergers and alliances, and in reasonably informed bets on near and medium term research and development market deliverables (Fischer, 2012, 2010). A Singapore sport is to count which pharmaceutical multinationals withdraw or invest locally, and in what they invest.

There was a stir when Eli Lilly withdrew from Biopolis in 2010 seemingly to be replaced by a major investment by Proctor and Gamble, seen by cynics as a move towards cosmetics and less serious science. In 2013, signals again were mixed when

Pfizer changed course, closing its dedicated clinical research unit at Raffles Hospital (a \$67 million facility with 54 beds, 70 doctors, nurses, pharmacists, and clinical trial technicians), part of a larger divestment from research and development under a new CEO (from \$9.4 billion in 2010 to 6.5 billion in 2012 after merging with Wyeth) and large-scale lay-offs. Pfizer maintained clinical trials with two Singapore hospitals, but its main presence was its Singapore manufacturing plant. Counterbalancing Pfizer, however, was the announcement by Novartis, whose R&D budget remained over \$9 billion, and which maintains an Institute of Tropical Diseases at Biopolis, that it would build a large, new state-of-the-art \$500 million biologics plant in Singapore, and promised to cross-train recruits in all four of its Singapore plants, giving them unique qualifications for the future. (The four plants are pharmaceutical manufacturing, two Alcon eye products plants, and the biologics plant.) Amgen likewise announced a \$200 million biologics plant in Singapore. Roche was the first to build a biologics plant in Singapore in 2009; and to date the industry provides 1,700 jobs. To prepare for some 500-700 new jobs in biologics, the Economic Development Board (EDB) and Work Development Agency created a Development and Apprenticeship Program (“DNA”) for on-the-job training of 180 people in 2013 at existing plants; since 2007, it had sent 270 PhDs and MSc degree holders to train in overseas biologics plants.^{iv}

The focus on the cell accounts for some of GIS’ new collaborations and licenses. In Feb 2013 the journal *Developmental Cell* published a new technique from GIS’s Shyam Prabhakar which requires only a few thousand cells to identify changes caused by chemical compounds that modify the genome (“or epigenetic changes”), where previously one needed one to ten million cells. This technique is now licensed to the local biotech S.G. Microlab Devices. Earlier in December 2012 the trade journal *Genetic Engineering and Biotech* took note of a new GIS-Fluidigm Single-Cell Omics Center (SCOC), the first in Asia, and intended (a) to act as an accelerant for GIS’s “track record of publishing breakthroughs based upon single-cell research”, (b) to stimulate more single-cell genomics across Singapore and Asia, and (c) to “provide single-cell analytics for drug discovery firms, pharmaceutical and biotech companies, academia, and clinics.” A first GIS research project using

SCOC, led by Paul Robson, aimed to define a minimal set of signaling and regulatory genes capable of defining the attractor and transitional cellular states that are needed early in human development. A similar center was established by Fluidigm at the Broad Institute in Cambridge, Mass., in May 2012.

This was also the era of a major turn in Singapore and globally towards neuroscience research and claims that this would be the “decade of the brain”. It was only in 1996 that the *Global Burden of Disease Study* (sponsored by the World Bank and the World Health Organization), to the shock and disbelief of many health policy practitioners, identified neuropsychiatric diseases as the leading cause of global disease burden, with enormous costs to national economies, as well as to the affected individuals and their care givers. This calculation was measured by including not just premature mortality normalized against expected life spans, but also *healthy years of life lost to disability*. In terms of life course diagnoses these burdens occur in *early life* (autism with consequent learning impairment, and, when severe, life time disabilities), in *late teen years and young adult life* (schizophrenia onset is usually diagnosed from late teens into early 30s, just when families have made maximum investment in education), and *end of life* neurodegenerative disorders (with chronic or relapsing course). With the aging of the world population, it is estimated that by 2050 over 20% of the population will be over 60. This is already the case in countries such as Japan and Singapore. There will be something like 150 million cases of Alzheimers, something that could be unsustainable for public health care systems as well as families, especially given the care-giver burdens.

The pharmaceutical industry, however, was shutting down its neuroscience research and exiting psychiatry. A few Alzheimer’s drug trials were in process, but if they failed, their pharmaceutical sponsors would also exit. A key reason is that drug discovery in this arena has been unsuccessful. The pharmaceutical industry has made large profits off of new drugs that have provided some increased tolerability and safety, but no fundamentally new mechanisms of molecular action. Ironically most of the drugs we still use were discovered in the 1950s by accident, were tested immediately on humans in ways that would be unthinkable under IRB

and clinical trial protocols today, with no notion of their mode of action. Lithium remains a first line treatment for bipolar disorder. The SSRIs, Prozac, Zoloft, etc., are safer and more tolerable than the first generation of anti-depressants but no more efficacious. Harvard's Steven Heyman, an advisor to the Singapore Bioethics Advisory Committee pointed out in January 2013 talk at the National University of Singapore, "All the commonly used psychiatric drugs today are no different from the prototype compounds of the 1950s: 1949 Lithium; 1950 Chlorpromazine; 1957 the tricyclic Imipranine, MAOI imipromiazid,... the first of the benzodiazepines, Chlorproxiolam was also discovered accidentally in 1957 at Ciba Geigy," quoted in Fischer 2013b). When the European Medical Association said it would no longer approve drugs that did not demonstrate a new mechanism of action or target a specific biomarker, pharma said they did not know how to do that (a case of market failure). While societies cannot force private companies to work on a public good, the social contract of modern governance includes health care for citizens. Indeed in some countries such as Brazil, health care is a constitutional right (even if the country has yet to figure out how to fund the obligation thus created, and this has become a vigorous arena of law suits and judicial activism), and elsewhere there are social movements advocating health care as a human right.

For these reasons as well as due to promising scientific and technological developments, neuroscience has become one of the hot new priorities of government investment, including in the U.S., U.K., E.U., Canada, and also Singapore.^v In Singapore, neuroscience was identified in 2007 as one of five areas of research priority by the International Advisory Council of the Biomedical Sciences Initiative. In 2013, the National Research Foundation funded a \$25 million five year Singapore Translation and Clinical Research in Psychosis Program. At NUS, the new SINAPSE (Singapore Institute for Neurotechnology), funded by NUS, A*STAR and the Ministry of Defense, was awarded a \$10 million grant over five years. At the same time, Singapore's Bioethics Advisory Committee launched discussions and issued a White Paper on the potential ethical issues that may emerge with developments in neuroscience (Fischer 2013b; BAC, 2013), and one of its members, the Chair of

Ethics at the NUS Medical School, advised the Necessary Theater on a play that addressed questions of genetic engineering.

Neural stem cells are among the hot topics in stem cell biology; we are still at the stage of learning through induced pluripotent stem cells, made from adult skin and other cells, how to make neural cells, stabilize them, and integrate them with other cells into functional therapies. The hope is to be able to inject, engraft, or engineer them to correct an identified genetic defect. Stem cell therapy clinical trials for disabled stroke victims began in November 2010 in Scotland. But this is fraught territory as yet: one needs to watch for tumor development, inappropriate stem cell migration, virus infection, and immune rejection. These are not reasons to stop, but on the contrary the biology challenge is to learn how and why these things might occur and how to short circuit, avoid, or counter them, or how to proceed otherwise. In the meantime, GIS continues to work in the fast moving field of blood stem cells and lung repair stem cells.

Looking Ahead 2015-2020

GIS is something like a bonsai, says the director: you plant and shape it, and let it grow in all directions, and then begin to reshape it. An important direction is the growing importance of computation in molecular biology, and in the past three and a half years, the number of principal investigators on the computational side of the Institute has grown from four to nine (out of a total of 26 principal investigators). A longer term goal is gradually finding cross-trained individuals who bring dual skill sets of the wet lab and computation. Already, of course, the computational folks are deeply informed in the biology: one cannot just hire a computer scientist and ask for help in analyzing biological data (we are long past that era). While people with such double skill sets are still rare, GIS's young recruits are among those who are developing tools that open up new biological vistas. One of the new senior research scientists (with BS from Anhui, MS from Cornell, Ph.D. from Berkeley, and postdocs both at Berkeley and at the Chinese Academy of Sciences) brings skills in evolutionary biology applicable to not just species (dogs and rice in Southeast Asia in his case) but to viral and microbial evolution (codon-

based likelihood methods in influenza and Human Papilloma Virus), and perhaps most importantly cancer genomics (given GIS's strength in cancer biology). Tumors are not unified or uniform groups of cells, there is a mode of constant selection in the tumor itself, so by looking at different regions of the tumor he attempts to figure out how the evolution takes place. Another new senior research scientist, also China-, and then U.S.-, trained, is a biostatistician, who already as a postdoc at Michigan implemented new software tools for rare variants in next generation sequencing data, to enable accurate ancestry estimation for samples with extremely low coverage sequencing data, and thus provide critical information to control for population stratification in downstream analyses in disease as well as ancestry studies. A third new senior research scientist, a Georgian with a Japanese Ph.D. and postdoc experience in the U.S., has been hired to develop diagnostic assays and thus help create a complete pipeline from basic upstream science to downstream translation (i.e., uptake by companies, or clinical use). Working with the Polaris platform, he is in a sense a "translation" specialist. A fourth new member of the Institute, is a German with a PhD from the Max Planck Institute in Berlin, who came first as a postdoc, and almost immediately scored a *Nature Cell* paper; and then within six months of becoming an independent Fellow with his own lab, published a *Cell Stem Cell* paper analyzing public data and finding that there are classes of genetic repeats expressed in defined early development of human embryos. He seems to have an amazing ability to find patterns that others have overlooked.

An important component of GIS's new hires is creating positions for returning Singaporean A*STAR scholars. These are the best of the best of Singapore's new pipeline of PhD and postdocs trained in high profile labs abroad, a pipe line of now some 1200 scientists, a program started by visionary founding director of A*STAR, Philip Yeo. Three of these are now Fellows or senior research scientists at GIS. One comes from Howard Chang's lab at Stanford, one from George Daley's and Lewis Cantley's labs at Harvard, and one from Robert Weinberg's lab at MIT Whitehead Institute.) The first already produced, while at Stanford, a *Nature* paper as first author and co-corresponding author, and is developing a high through-put approach to understand the structure of RNA, which unlike DNA (a

linear double helix structure), folds into domains and requires new techniques to probe. She promises to become a leader in this field, and already has won a prestigious Branco Weiss Fellowship grant. She does wet lab work, and thus needs to work closely with computational people, a capacity in which GIS has now been building strength. The second comes with six papers on which he is first author and a corresponding author (plus six other papers). He works on muscle stem cell metabolism during regeneration and aging. The ability to modulate metabolic networks to regulate stem cell proliferation and differentiation is directed towards treating degenerative diseases. The third has a Ph.D. from GIS (NUS) in Bing Lim's lab, and then went to postdoc with Weinberg at MIT, and works on targeting cancer stem cells.

Aside from the principal investigators, as the last indicates, GIS is also a training institute with currently 89 postdocs (including 41 women), graduate students, and a few undergraduates working on degrees at local universities. The postdocs come with Ph.D.s from Singapore (24 from NUS, 3 from NTU), the U.S. (21), China (10), the UK (7) Germany (5), India (3), France (2), Italy (2), and one each from Australia (Melbourne), Austria (Vienna), Canada (Montreal), Spain (Madrid), Netherlands (Utrecht), Russia (Volgograd), Sweden (Umea), Taiwan (National Cheng Kung), and Turkey (Koc). They include eight with first degrees from India, at least nine from China, one from Indonesia, one from Malaysia, one from the Philippines, and one from Sri Lanka. Inferring from names and first degrees, of the 89, thirty-nine are Singaporean nationals, 18 are Chinese nationals, 15 are Europeans including one Turk and one Russian, 11 are Indian nationals, and the rest are Southeast Asians from the Philippines, Indonesia, Malaysia, and Sri Lanka. PhD students also come from Iran, and one was recently from Vietnam, now postdoc'ing at Harvard.

What interests me in these brief notes in what GIS director calls a now mature Institute, is its international character, its fulfilling of the promise to train cohorts of local Singaporeans, and its ability to place its graduates and recruit from top global labs, as well as recruit from lesser known universities and place those individuals into its own networks. Although Cambridge, Imperial College, Harvard,

Stanford, Berkeley, UCSF, and MIT remain prominent, it is interesting that the current posdocs have PhD degrees from 19 U.S. universities, eight Chinese ones, five German ones, four U.K. ones, two Indian ones. Tracing out finer grained mentorship and expertise networks is beyond the scope of this essay, but aside from the names already mentioned of specific key labs, it can be noted that for instance, while Montreal is the home of a former member of GIS in computational biology with French training and some other of the selections of postdocs suggest similar connections, other selections of postdocs by P.I.s cannot be easily guessed, and would require direct elicitation. It is to one such elicitation, that we now turn, albeit with a different genome institute in mind.

II. *BGI: Mapping Life in/from China, 2013.*

It is not surprising that life histories and institutional ones follow each other around like a Moebius strip. Life histories can be hieroglyphs of social formations. They can provide cross-sections through shifts in the social order. The case of Wang Jian, one of the co-founders of BGI reads like a metaphor or a hieroglyph for both contemporary China and BGI. His co-founder, Yang Huanming, and his former student and successor as CEO, Wang Jun give further dimensionality to his trajectory and that of genomic sciences in China and globally. That trajectory leads from the Cultural Revolution when Wang Jian was twelve, and his parents, although Party members, were incarcerated. It leads to the American histories of the Human Genome Project; and then back to China of the 1990s and 2000s. Wang Jian is a long distance runner in both senses: as a runner in the movement across the major moments in the history of genomics, and as one who continues to bicycle to work and has climbed Mt. Everest to the final base camp. Thanks to the turmoil of the twentieth century, he has gained a sense of humor about the obstacles in life.

There is an enormous amount of mythology about BGI, the largest genome sequencing center in the world. The myths are noir projections deploying simplistic master narratives of state competitions, rather like Roland Barthes describes the allure of the good and evil mythologies of television wrestling. But in historical

reality, BGI is as much a creation of Danish and U.S. scientific networks as of internal Chinese ones.^{vi} BGI built itself despite the indifference of the Chinese state and the hostility of older Chinese scientific institutions such as the Chinese Academy of Sciences. Only when it gained fame abroad with President Bill Clinton's announcement on 23 June 2000 of the completion of the first draft of the Human Genome, mentioning China's role in sequencing 1% of the Human Genome, did the Chinese state take note.^{vii} Since then BGI continues to maintain its distance from the Chinese state and bureaucracy, and is now primarily located in Shenzhen on the border with Hong Kong, with most of its machinery and data storage servers on the Hong Kong side. Thus it is *BGI*, no longer the "Beijing Genome Institute." The history of the permutations of the letters actually tracks Wang Jian's efforts to build, as he jokingly puts it, a Golden Gate bridge between Beijing and the U.S. The diagnostics company that he established upon his return to China, the unsuccessful effort to build a genomics institute within the Chinese Academy of Science (or its fragmenting into separate units), and the effort to establish the current genomics powerhouse in Shenzhen with offices and collaborations across China and the globe are variously BGI, BIG, or IBG, no doubt with further variations in Mandarin ("Huada") and the Chinese writing system. Indeed STS scholar Haidan Chen^{viii} tells me that Hua (China) + da (big) is the short handle for Huada Jinyin (genome) Yanjiuyan (Institute). So Beijing has been replaced by China Big which is partly a play on the English acronyms and partly a statement of divorce and independence from the failed effort to build an institute within the Chinese Academy of Sciences in Beijing, and a claim to being China's biggest genome center.

The voices of Yang Huanming and Wang *Jun* provide further dimensions both to international networks and collaborations, and on the differences across three generations of BGI staff and the training of a new generation of Chinese genomicists and bioinformaticians. Yang Huanming and Wan *Jian* are of the generation that went through the disruption of Chinese universities by the Cultural Revolution, and then training in Western ones. Wang *Jun*, now CEO of BGI, also took a degree at Peking University (under Wang Jian, having turned down an offer from Stanford) but already was among a younger generation impatient with sclerotic institutional

training in fields where youthful talent could be trained directly on the job, and could make breakthroughs in new fast changing fields (not unlike the careers of such luminaries in other parts of the information technology revolution like Bill Gates of Microsoft, Steve Jobs of Apple, and later Mark Zuckerberg of Facebook). Today BGI is beginning its own Academy for training its personnel which eventually will be a degree-granting institution. The average age of BGI's four thousand employees is 26, and for the scientific group it is under 24, "so it is lots of young kids" (Wang Jun, MF interview April 2013).

This is admittedly a transition with its own challenges, as is the effort to set up not just service organizations across the globe, but more importantly data collecting operations across China that can be trusted to produce quality standardized samples and information. One works with what one has, and with *persistence*, a term that becomes a refrain in these stories, one produces new scientific horizons beyond current scientific capacities. In BGI's case, the persistence has to do with proving the value of what Samir Brahmachari, the Director of India's Council for Scientific and Industrial Research, called in mock (or real) scepticism "data-intensive discovery" rather than hypothesis-driven discovery." In an amusing exchange, challenging CEO Wang Jun at the 2013 Human Genome Meetings in Singapore, Brahmachari asked,

Great talk. You know this reminds me of a talk seven or eight years back when we said that we need 20,000 samples, then 45,000. Today less than 10% we understand from the type 2 diabetes from the DNA sample. Now you are saying let's go and do 100,000 or more samples. Do you think this approach is the only solution or we have to sit back and now ask at the last slide of yours saying it is so complex, let's go back and do **hypothesis-driven discovery**, rather than **data-intensive** discovery. Data intensive discovery means data will speak, it'll converge, it will come out of its own pattern, and from the pattern we should be able to interpret. It looks to me variation is multi-layer, multi-dimensional. When do you go back to hypothesis-driven discovery, what's your view?

A: Thank you Samir, I am very **persistent**. Also BGI is very persistent. So I don't say we will go back (audience chuckles) to the traditional way of doing the way we started with type 2 diabetes for example. So we are going to generate at least a body [of data], eventually getting **genome data together with the phenotype data**, so people will figure out what's going on there. So if it is not BGI, some people will figure out what's going on there with those data results. And we're just going to do it. We have to do it. There is **no shortcut**, there is no turning back, we just have to be persistent.

Samir: I completely agree. I [did] not say turning back, I would say looking on the 30,000 feet level. See we are all used to thinking that we will find . . . we'll find the gene and we'll get it. Now you only brought back to the last slide, we have to look at 30,000 feet, holistically look at the **human individual with his bacterial composition**, with his **genetic predisposition**, his **environmental effect** and the **food habit**. Now **how to model this** in with respect to the data we are generating? How [do] we connect this model to the data because we go back eventually by one element by element analysis we are not going to ...

A: Yeah, I think there is a quick answer to that question. If you really want to review the world at 30,000 feet it is not going to be enough, you have to go to outer space to watch the entire earth and this is the answer.

At issue in this exchange is the strategy of stratified medicine or better targeting of why drugs work for some patients and not others, leading it is hoped eventually to personalized medicine, therapies that take into account an individual's particular make up: his or her genetics as well as habits, diets, and travels through

microbiotic fields. The example Wang Jun used in his talk on BGI's current research and its "dream-line" strategies for the future was Type 2 Diabetes (T2B) in China. He went on to say that we still talk of T2B as if it were one phenotype, but now with the ability to look at not just genomics, but proteomics, metabolomics, and, especially, now gut bacterial communities, we should be able to stratify T2D into thousands of types so that one can then go back and look at the genetics and get more significant statistics that can target different therapies for different groups or individuals. This is no minor matter: thirty years ago, the prevalence of T2D in China was less than 1%, 0.6-7% of the adult population; in 2012 it was over 10% and pre-diabetics were another 15%. So a quarter of the adult Chinese population is either diabetic or pre-diabetic. (This gathering storm, of enormous concern for health care budgets, interestingly is almost identical in numbers and distribution to the gathering storm of chronic obstructive pulmonary disease [Rebuck et al., 2013]).

Studies being conducted by BGI, Copenhagen University, and Novo Nordisk Foundation Center for Basic Metabolic Research, and in association with the MetaHIT Consortium in Europe have begun identifying biomarkers in the bacterial colonies of the gut for diabetes and other diseases. At issue is the ability to correlate or triangulate a series of different kinds of analyses, with the promise of faster and earlier diagnosis targeted for particular individuals. As Brahmachari acknowledged, T2B is a heterogeneous and multifactorial disease (as is COPD). Pathogens in the gut moreover are less like individual causes than balances of bacterial ecologies whose therapies might involve rebalancing rather than trying to eliminate a bacterium or class of bacteria. BGI sequenced the intestinal bacteria of 345 people in China, of whom 175 are diabetics to seek out differences that make a difference. Similar work is being done in Denmark and across Europe. A second step in confirming findings is to grow bacteria from mice with diabetes to see which or what imbalance might cause diabetes. The intestinal microbiome or bacteria (which vastly outnumber the human cells in our bodies) is, as Wang Jun and others put it, our "second genome", and understanding its effects on our bodies, he argues, might well herald the era of personalized medicine, as well as gentler, more holistic therapies "in the not too distant future". "Holistic" here, as Wang Jian's biography

makes clear, is one of those semantic switches that can signify an openness to traditional Chinese (and other) medicine (TCM), or on the contrary an insistence on the difficult work of actually tracing out the multiple interconnections that compose our biologies and ecologies.

While the exchange between Brahmachari and Wang is amusing and good-natured, there is an underlying irritation from BGI leaders who know well that their colleagues have often tried to position them as ‘research without scientific questions,’ ‘no brain only have muscle; do the dirty work’; ‘we [in the West] do science, you do the dirty work, just sequencing.’ These phrases can be self-serving and ethnocentric, but the self-servingness is also an active *tactic* of marginalizing. BGI leaders cite these phrases now both as badge of honor (of systematically overcoming obstacles and working up the scientific as well as commercial value chain) and as lingering irritation at the continued struggle for recognition (which today they are finally achieving, and in the process bringing to Philadelphia and Davis models of integrative collaboration). BGI has branches and offices now in Shanghai, Hangzhou, Wuhan, Beijing, Hong Kong, Tibet (studying the adaptations to high altitude), Davis, California (agricultural projects), and Philadelphia (medical projects).

BGI leaders have been insiders to the international genomics projects from the very beginning as junior academics at the University of Washington (with Maynard Olson, Lee Roy Hood, and Bob Waterson; tapping Bill Gates as a funder, Eric Lander as a visitor and advisor) and the University of Copenhagen (where Yang Huang Ming got his PhD, Wang Jun is now Professor of Genetics, and other junior leaders have also gotten PhDs). These mentorships and networks have supported the initiatives of BGI to get off the ground. One of the key connections through this network was to secure the support of John Weston, the CEO of Solexa, to loan or rent sequencing machines when BGI had essentially no money, on the promise that service work would allow them to pay Solexa back, and to make this agreement survive the sale of Solexa to Illumina. Another earlier important connection was the provision of earlier (first) generation sequencing technology by the Wellcome-Sanger Trust.

It is the case, of course, that as BGI has grown that it has had to face competitive moves even from previous supporters. Illumina, eyeing the Chinese market, apparently with the help of the U.S. Commerce Department, blocked the use of its machines for medical research inside China. BGI's response in 2013 was to buy Complete Genomics, an American company with its own proprietary sequencing technology.^{ix}

Yang Huanming, in his 2011 Y.T. Chen Distinguished Achievement Award at the Human Genome Meetings in Dubai, reminded the audience, "Please don't think that we got a lot of funding" to do the 1% of the Human Genome, or "that we were regarded as heroes". Both Yang and Wang Jian delight in recalling that when the June 2000 draft of the Human Genome was announced by President Clinton acknowledging the contribution of "Chinese scientists", the Chinese political leadership, particularly President Hu Jin Tao, responded with "what?" and "who?". It was, Yang reminds with pride, "the first large scale genomics implementation in the third world," in an underdeveloped country outside the U.S., Europe, or Japan. Before moving from Beijing to Shenzhen, there was a period they moved to Hangzhou, near Yang's hometown of Wenzhou,^x and worked very hard on the rice genome.^{xi} Laughter erupted when, saying, "I want to show pictures of how hard they were working, but how tired they were," he showed a slide of his young staff slumped over workstations in exhaustion. "This team deserves enormous credit for their outstanding world class accomplishment. Thank you *Science* magazine" (which published the rice genome as a cover story in 2002). The list of accomplishments after moving to Shenzhen and using the new generation of sequencing machines: participating in the HapMap Consortium, joining with the Danes in a pig genome project, sequencing the first Asian human genome in 2008, joining with colleagues in the U.S. initiating the hundred (later thousand) genomes project, working on the silkworm genome, maize, cucumber, two kinds of ants, with Saudi Arabia on the camel genome, and so on. Like Wang Jun, Yang stresses the role of persistence, building self-confidence through achieving things people said they could not do, "jump starting" genomics in a third world country by participating in international consortia, and taking risks, especially financial risks in the beginning. BGI was

really too poor to do even 1% of the human genome, and had to borrow four sequencers, four million RMB from the staff, and 12 million elsewhere (including from the mayor of his hometown, plus a major chunk from a small diagnostics company that Wang Jian had founded upon his return from the U.S.) Again they borrowed 60million RMB to initiate the Rice Genome sequencing before the funding arrived. It was dangerous, it was risky.

Yang ended his address with a call for international free and open sharing of genomic data which is the common heritage of all mankind (and should be the common ownership of all), and for using new genomic knowledge for social good. He noted, again as he had in a jointly authored article on BGI, that no institute or country can do this research alone, that all the animal model genomes were done by international consortia, that BGI had immediately put the rice genome in the public domain, helped with the SARS crisis (when finally allowed access to samples from the Army Medical Hospital in Beijing, they identified the strains, provided diagnostic kits), and forensically analyzed the DNA of victims of the 12 May 2008 earthquake in Sichuan. He acknowledged in particular the help of the Wellcome Trust Sanger Institute in providing sequencing equipment early on. His professor Mas Kuland (Copenhagen) now spends several months a year at BGI.

In the following section, I follow Wang *Jian's* story as an indexical thread in the social transformations of twentieth and twenty-first century China (and the U.S.); in the final section, I return to Wang *Jun's* “dream-lines” or strategies for the future as a current analysis of where we are with the promises of genomics for helping create a more stratified, and even personalized practice of medicine.

The Charismatic Voice of Wang Jian, April 2013.

When asked where the story of BGI began, Wang Jian replies without hesitation, in Seattle at the University of Washington. Or for him, it also begins around the time “when Bill Gates was starting his business, [and] I was being re-educated in the country-side”. Gates is one year his junior. As it so happens Jian had just had dinner and a four hour conversation with Gates the previous evening in Hong Kong about future directions and joint projects, when I interviewed him at BGI

in Shenzhen in April 2013. After the chaos of the Cultural Revolution, and refusing a scholarship to study and train in sports, Jian went to the Hunan-Yale medical school, Hsiang-ya or Xiang-ya (ya meaning Yale), founded in 1901 and supported by the Rockefeller Foundation. Under Mao it was simply the Hunan Medical School, but in recent decades it got its name back, and the associated Middle School again became Ya-li (yale + li, “civility”). After that Jian attempted to train in TCM (traditional Chinese medicine), but that didn’t last, and determinedly teaching himself English, he managed to get some publications in English, enough to get invited to the University of Texas Medical Branch at Galveston, then Ohio State, and eventually the University of Washington where the ideas of the Human Genome Project were being formulated by Maynard Olson, Leroy Hood, and Robert Waterson. Olson and Hood fought. Hood left the University of Washington to start his own institute, with funding from Gates. Later, in 2001 Waterson was brought in from the Washington University in St. Louis to head a Department of Genome Sciences formed by merging the Departments of Genetics and Molecular Biotechnology. It was Maynard Olson who encouraged Wang Jian to start something in China.

I follow Jian’s account in two rounds, the one having to do with the institutional history, the other having to do with the trajectory in China before Seattle as Jian’s generation emerges from the Cultural Revolution.

The Institutional History

So where does the BGI story begin? Jian replies: *“in Seattle at the University of Washington.”*^{xii} Jian was working with Maynard Olson and Leroy Hood. Both had come in 1992, Hood from CalTech, Olson returning to the University of Washington from time at Washington University in St. Louis, where Robert Waterson had founded a Genome Center in 1993. Hood and Olson *“started a new department called Molecular Biotech and invited lots of top leaders because Bill Gates paid the money, and then when Maynard also was there started the Genome Center.”* Olson had created a way of breaking genomes into manageable pieces, applied it to the yeast genome, and helped make the human genome project a possibility. David

Botstein put it this way, "He allowed us to mechanize, computerize and organize the process. Maynard was one of the top two or three key brains behind the Human Genome Project" [HGP] on the occasion of Olson being awarded the Gruber Prize (which Botstein had been given a few years earlier). Olson's construction of a high-resolution physical map of yeast was a key step leading to the plan for sequencing the Human Genome. He also served on the initial Alberts Committee of the National Research Council, which issued the report "Mapping and Sequencing the Human Genome" which led to the HGP. Meanwhile at CalTech Leroy Hood *"was the one who invented the four-color labeling ACTG.^{xiii} So there are two guys, two top guys there, and in the early days they were the best. Eric Lander went there a couple of times to learn all these details. He was a young guy at that time (laughs), he was a newcomer.^{xiv} So they started the Molecular Biotech Department and when Maynard was also there they started the Genome Center."*

*"And Maynard Olson encouraged us to set up a genome lab back in China. He was the first one to support that kind of idea. So we started talking about this in 1993 or 92. George H.W. Bush had launched the HGP, I think in 1990, [actually in 1989 he signed into law the appropriations for the Human Genome Project] announced they were going to do it. 1997 was the speed up, but 1990 announced it, and for 8-10 years was the physical maps, and then when it really came to the sequencing, Eric Lander jumped in [after] Craig Venter said we can use the shotgun [method of sequencing rough and quick fragments and then reassembling them, rather than proceeding more systematically and slowly in a linear way], and Eric is the math person and easy to catch up with that kind of shotgun ideas, he know how to use the computers, surpassing all these biologists and became the number one leader for the Human Genome Project. He was the guy [able] to compete with Craig Venter. The guy behind Venter, the math guy, is the guy from the university of Arizona, forgot his name. So all of the math matters. 1997 or 98 those guys: Lander and Bob Waterson. At that time **the largest** genome center was in St. Louis, at Wash U. That was the biggest one. But in the beginning the University of Washington (Seattle) was **the best** one, and then Lee Hood and Maynard Olson started fighting inside and destroyed the whole system.*

And then Lee Hood was kicked out by the university and started his own Institute for Systems Biology.

That's a long story. So we decided wow, wow, wow, we are not going to get involved with the political things of inside fighting, so we decided, come back [to China] and started our own genome project. But all those big guys said yes, they supported us.

This was in 1996 when Jian and Yang Huanming first started writing proposals. "We really started working and lobbying the Chinese government in 1997, and in 1998 the first lab was established in the Chinese Academy of Sciences.

But when we wanted to join the Human Genome Project, we could get no answers from them (pointing upstairs "not allowed to mention their name" "in the north"). So we left the Chinese Academy of Science, CAS, and started BGI. 1999. Sept 9, 1999, 9 o'clock, 9 am, 9 seconds (laughs) just for fun. So the first target was 1% of the Human Genome Project.

How did you get the money to get sequencers, or had you gotten that already at CAS?

*No, no, no. We did not have any money, if we had gotten money in CAS we would not have left it. But we could proceed because **nobody said yes, nobody said no**. This is a tricky thing. If the government had said no, then we would have had problems. I'm going to remember who said no to us, right? There was no yes and no no. No response.*

OK, so how did you get started?

Yang Huanming got a couple of million from his home town local government, his cousin was the mayor (laughs), and then the mayor got into big trouble (laughs). And I got a couple of million from the small company I had started, a diagnostic company. They had started making money at the time, so I got money from the company. So the money come from both Yang Huanming and from my company, 13 or 14 million. We used that money to pay for a quarter of the machines. Another 70% we promised to pay them back as rental fees. But we used most of the money to buy the

reagents. We knew we had to have the reagents to get accomplish anything, to do at least 50 or 60% of the task. We calculated before we die, we should finish at least a half of the project. The gamble on the machines was that there was no reason to waste money on them. They could just take them away from us, if we could not find the money, but they too were waiting to see if we succeed, they would get their money. I was really gambling they cannot sell, they just waiting for the final day, the real victory come in they get the money (laughs). But I was gambling that Jiang Zemin [President 1993-2003] would eventually support us. I bet on it. And finally he did. When Bill Clinton said thanks to the Chinese scientists who also contributed to the Human Genome, Jiang Zemin began looking for "who did it?!" Then he came down to visit us.

The northern and southern centers of CAS then claimed some credit, and Jiang said they could have credit, but after ten years no body remembers them, the National Genome Center, North and South. They are gone, like lots of U.S. genome centers, erased from memory. The human genome map was declared finished in 2003. It was sort of complete, it's never complete, they just call it the final map.

So the next project was the HAP map?

Yes, the HAP map. Eric Lander talked to Wang Jun and we got money and we did 10% of the HAP map. We invited Lander to Beijing to support us and asked him to talk direct for us to the top leader, the big whohoo we call him. That worked. Eric Lander he comes to us every 3-4 years. Our young guys in Boston stay in his house.

So what happened between 1999 and 2007 when BGI moved to Shenzhen?

In 1999 we left CAS and started BGI, and in 2003 the President, Hu Jian Tao, came to visit us and approved of what we were doing. So then the Chinese Academy of Sciences created a new institute for us called BIG, B – I – G (laughs). We did not want to change [the name] BGI. We had a feeling some day we are going to start fighting just like Maynard and Lee Hood (laughs), so we keep the old BGI under the table, and outside we use BIG. We promised the President that we would do our best to make a world class genome center. So everybody was happy. But when the big boss left, there

was no real financial support. Instead there was lots of argument in the scientific community [why give money to this?] Yeah, because this is stupid, dirty job, just the sequencing, it is low level, it is just large scale, it is not real research. They called it some research without scientific questions. So we said, OK, we have no brain, we are stupid, blah blah blah.

After two years of this, we had gotten zero funding from the competitive grants. We just got the basic support for the Institute. It is kind of the Chinese way: they give you overhead for your basic survival. You get salary, you get money to pay the electricity. But then you have no money to buy the equipment and the reagents, and you can barely survive. Some people like that, they don't care whether they have publications or not; they are content to just set up a few joint projects and just be the follower. In 2007, we quit, divorced. I still have the BGI, but I know I am going to have very difficult time if we stay in Beijing, so I left and came naked running from Beijing to here. We brought nothing. We came empty handed. That means we are not taking any government property, nothing. Otherwise we were going to have big trouble. We still thinking crazy, big things. And we, special thanks to Bob Waterson, I remember it was 2000, 2001, he moved from Wash U to U Wash. He is a very close buddy of Maynard Olson. He reorganized things and created the first department of Genome Sciences, putting together the Genetics Department, the [Molecular] Biotechnology Department, and the Genome Center.

We have very close relations. Every time we had some idea some crazy idea we would come to these big guys, these pioneers, to help us with their advice. They suggested why not sequence a single Chinese to compare what is different. It might be a good idea, but we did not have money to do that. Nobody thought it necessary because such there would be such a small percentage difference. There is no reason to sequence a Chinese. All of us come from Africa so we have the same ancestors, why do a different genome? Crazies. You are crazy.

Well [we said, let's] just take a look. See, we're just curious (laughter). That means research without scientific questions. That means we are stupid (laughs). So, and then for a long time, we called ourselves 'no brain only have muscle. Do the dirty

work because we have no brain. And make other people happy [by just providing sequencing services for fees]. Ok, you have no brain, do whatever you want.

So who gave you the money to do it?

No. No money again. It's the same game, we play the same game. We came over here [to Shenzhen], the local government said they had a building [an empty former shoe factory] here and maybe they would give it to us for two or three years for free and if we produced something good, maybe they would pay the bill for BGI. Then we met John Weston, who was CEO of Solexa and he lent five, five or six, machines and we promised to pay for them in two or three years. Then he sold the company to Illumina, he got 30 million bonus for himself. . . . We paid them back month by month. After two or three months, in six months, we paid back all the money [by doing free for service sequencing]. When we did the first Asian genome, we made the mayor and President Hu Jin Tao so happy, they paid us \$20 million for four years. In the beginning the deal was 30 million RMB total, but the beautiful cover story of the first Asian genome map, made them so happy [they gave a bonus]. This was the first Nature article produced in Shenzhen. For thirty years, they had no real science, now they had. It made them so happy, they paid us double. Twenty million per year for four years. Wow. Money come from the heaven. Thank God. I wished it would keep going that way. But there is no way: after four years stop. Stop raining. Never mind. By then we could support ourselves by doing fee for service."

Having misheard 'Soviets' instead of 'service,' Jian corrected me and then commented that they tried to involve Russian scientists, the Russian Academy of Sciences sent delegations twice. *They have math expertise, but they couldn't decide. It is a puzzle because although Russia is far behind in biology, all the software people at the Sanger Institute in England are Russian, also in Craig Venter's group. But when BGI tried to recruit some of them, they declined saying salaries are better in the U.S.*

So, instead of bringing American based scientists to China, BGI began opening offices in the United States. The Children's Hospital of Philadelphia (CHOP) was the first, then one at the University of California, Davis.^{xv} Wang Jian, however, stresses that it was the American *institutions who came to BGI, not the other way around.*

With a bit of humor, he says, "They came to us, first CHOP. All these joint labs outside of China, they come to us, 'say hey can you help us?' Wow, sounds interesting. Can you do the communist way? What is communist way -- you supply us, we put our people machines, we work together. Deal. Done, done. And [then] the Chancellor of U.C. Davis comes over, five minutes, deal is done. There is also an office in Cambridge, Mass., near the Broad Institute."

The point, to use Ulrich Beck's useful term, is that methodological nationalism (seeing everything through nation-state categories) can be misleading. The republic of science -- while hardly denying or ignoring national boundaries, intellectual property and other legal terrains and ethical review processes -- also maps across those political boundaries. It works through qualitatively structured networks, including mentorship and friendship lineages. Collaboration is as much about building these as about project outcomes and temporalities.

Conclusions

If there is utility in the kind of juxtaposition attempted in this essay, it is one of critically reevaluating history of ideas, institution-centric, nation-centric, or field-centric accounts of science in a globalized terrain. Much is to be gained by analysis of statistical flows of international students and postdocs, but much is also to be gained by a more fine grained analysis of actual networks, working collaborations, and exchange of ideas. If one stereotypically understands Singapore as having created a scientific community by importing "whale" (high profile, senior) scientists, and China as a series of state supported enterprises, this tale of two genome centers turns those stereotypes upside down. The newly enlarged scientific community in Singapore is the result of a concerted state initiative through the Economic and Development Board (EDB), A*STAR, the Ministry of Trade and Industry, the Ministry of Education, the Ministry of Health, and the National Research Foundation. Much of the initial infrastructure is credited to the visionary charismatic voice of Philip Yeo, who served as head of EDB and then A*STAR (Agency for Science, Technology and Research) and put in place the scholarships that sent some 1200 Singaporeans abroad for advanced education. Likewise the charismatic voice of Dr. Edison Liu

was critical to the establishment of the Genome Institute of Singapore, as was the earlier voice of Sydney Brenner in getting Singapore to focus on the life sciences as a possible economic engine for the next revolution after the computers/information technology one. The transition to a new institutional re-balancing between research universities, A*STAR (non-university research institutes), and the academic research hospitals at both NUHS (National University Hospital of Singapore) and the Duke-NUS graduate medical school affiliated with the Singapore General Hospital was likewise championed by the successor to Philip Yeo, Lim Chuan Poh, the head of A*STAR.^{xvi} At GIS, Singaporean scientist Huck Ng, who took over the reins from Edison Liu, guided the Institute through its restructuring and into its new collaborations.

Inversely, the explosive expansion of BGI on the world stage was, by Wang Jian's account, a national and international bootstrapping, despite the state. Not that BGI in the beginning did not try to get state support inside the Chinese Academy of Sciences, but establishments can be inertial, and BGI had to strike out on its own, even moving away from the center of power in Beijing. Here international networks proved critical in the bootstrapping, and continue to be so, albeit now the competitive pressures intensify, as do strategies to enter the market. One of the fascinations of globally distributed science is the internationalization both at the unit level of the laboratory (the analysis of postdocs at GIS is one such indicator), and at the level of collaborative-competitive races to gain credit and to move the field forward both in terms of biological understanding and in terms of translational therapeutics. In this sense too, science provides microcosms of larger social processes of migration, internationalization, cosmopolitical growth. It is a privileged one, on the leading edge, dealing with issues ahead of those faced by society at large.

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ⁱ I have been doing bits of ethnographic work in Singapore since 2009 beginning at the Genome Institute of Singapore thanks to the welcome offered by its then director, Dr. Edison Liu. He was then President of the Human Genome Organization, and through him, I was also able to attend a series of HUGOs annual meetings and other meetings over five years in a series of fascinating thematic programs on both the changing technologies and their work in fields ranging across health domains. At those meetings I met many of the leaders in genomics, including the leaders of BGI, and followed up with a visit to BGI in Shenzhen in 2013 where the interview with Wang Jian used in the second half of this essay was conducted, and also a briefer one with Wang Jun. This essay was presented originally at the Third Biopoleis conference hosted by Prof. Greg Clancey and Tembusu College at the National University of Singapore, 2013, and I gratefully acknowledge the feedback on the BGI portion of Haiden Chen (who has written a beautiful article on the

Kedourie biobank in Hong Kong, among other studies), Margaret Sleeboom-Faulkner (see her recent book 2014), and others; and of course to all the helpful friends and colleagues at GIS most acknowledged in the earlier essay that was originally presented in the First Biopoleis conference (Fischer 2013a) and I continue to be especially indebted to Lim Bing, Ng Huck Hui, Tam Wei Leong, Ng Shyh Chang, and Axel Hillmer.

ⁱⁱ On juxtaposition and multi-locale, see Marcus and Fischer 1986, on mosaic and multi-sited see Fischer 1990, 1994, on emergence and third spaces see Fischer 2003; on the scientific republic as fields of emergence, collaboration and competition, see Fischer 2013a; on the peopling of technologies, Fischer 2013c.

ⁱⁱⁱ There are many accounts of BGI, short interviews, and different summary characterizations. There is even one with a picture of Wang Jian and Wang Jun in black cowboy hats talking about the movement towards personalized genomics (<http://archive.sciencewatch.com/dr/nhp/2010/10marnhp/10marnhpWangET/>).

See also e.g. Hillers 2013, Lauerma 2012, Bloomberg Business Week accounts 2012a, 2012b, Biospectrum 2013, as well as the web page biographies of Yang Huanming, Ph.D. Copenhagen 1988, postdocs in France and the U.S.

(http://en.wikipedia.org/wiki/Yang_Huanming). Wang Jun: Ph.D. Peking University 2002, professorships at Copenhagen, Aarhus, Peking; CEO of BGI (http://bgiamericas.com/wp-content/themes/bgi/pdfs/Jun_Wang.pdf).

Wang Jian, Ph.D. Texas, postdocs at Iowa, Washington; Board Chairman, Beijing BGI-GBI Biotech Co., Ltd.; Director, BGI-Shenzhen (http://bgiamericas.com/wp-content/themes/bgi/pdfs/Wang_Jian.pdf).

^{iv} A recent item in the Straits Times (Lee 2015) adds the departure of GlaxoSmith-Kline's neural pathways discovery unit at Biopolis announced December 2014, and the expansion of Chugai Pharmabody Research established in 2012. The main story is still the joint steering committee of A*STAR and Merck which has selected 15 of 100 proposals from local scientists to support, under the headline "R&D health: Big pharma bets on Biopolis". A*STAR's development group director Jonathan Kua is

quoted as saying Biopolis works “with thirty pharma companies from around the world”, and has “about 30 new projects with these companies every year.”

^v Globally, the largest initiatives are: (1) the 2004 United States NIH *Blueprint for Neuroscience Research* to train a new generation of cross-disciplinary neuroscientists and develop a cooperative framework for institutes and centers;

(2) the 2010 boost in funding for the UK Brain Banks Network and research initiatives on risks of developing dementia in old age; (3) the establishment of the Canada Brain Research Fund with \$100 million matching funds from the Canadian government; (4) the billion euro, ten year, Human Brain Project, announced in January 2013 by the European Commission as one of its two lead Future Emerging Technologies (FET), the second being in materials sciences, a Graphene initiative. Each initiative involves researchers from at least 15 EU Member States and nearly 200 research institutes. The "Human Brain Project" will create the world's largest experimental facility for developing the most detailed model of the brain, for studying how the human brain works and ultimately to develop personalised treatment of neurological and related diseases. Funding will come from the Horizon 2020 program (2014-2020). (5) A U.S. project for a Brain Activity Map, to be funded at the same scale as the Human Genome Project, \$3 billion over ten years. (6) The 10 year \$100 million accelerated research initiative to study 1,000 retired National Football League players, funded by the NFL players' union, awarded to Harvard University (announced in January 2013). Over 100 concussion-related lawsuits have been filed against the league, with thousands of players claiming the NFL did not do enough to inform them of the long-term dangers from repeat brain injuries and protect them. Attention has focused on chronic traumatic encephalopathy, an Alzheimer's like condition (focusing on the tau protein lodged in the amygdala and hippocampus), and the potential of LED (light emitting diodes) for preventing permanent brain damage from concussions, suicides, erratic behavior and depression. The study will also attend to searing joint pain and heart problems linked to extreme strength training, and dramatically shorted life spans.

vi The anthropological demand for ethnographic specificity seeks to follow out the networks in particular fields and across events in order to understand structural changes at a finer granularity than just aggregate manpower figures. More than half a million Chinese students have been trained in the U.S., U.K Japan, France, Germany, Australia and Denmark, and a large number have returned to China (Wang Hongyi 2013). While many have noted numerical flows of this sort, it remains unclear where and how these returnees have been able to contribute, and there remains a good deal of concern that the best remain abroad, and that the talents of those who return are not always used in the best ways, or that the most accomplished and experienced in the actual practicalities of scientific management at best come part time keeping their jobs abroad should political winds shift. In this respect too, BGI provides a rather unique case of being able to both do domestic training and negotiate, government, NGO, and private corporate structures while also collaborating internationally. Indeed Wang Jun has reversed the relationship deployed by many diaspora Chinese by being Professor in Copenhagen while largely working from Shenzhen.

vii June 23, 2000 in the East Room of the White House. President Clinton's very first sentence acknowledged the Chinese scientists as distinct from the Chinese state, whose ambassador was not one of the state representatives of their government's contributions to the Project. He said: "Good Morning. I want to acknowledge Prime Minister Blair who will join us by satellite in just a moment from London. I want to welcome here the ambassadors from the United Kingdom, Japan, Germany, France, and I'd also like to acknowledge the contributions that not only their scientists but also scientists from China made to the vast international consortium that is the Human Genome Project." He went on to acknowledge Dr. Francis Collins, head of the International Human Genome Project, as well as Celera President Dr. Craig Venter, a private company whose pursuit of the shot-gun strategy of sequencing pieces of the genome to be later reassembled, based on new high-through-put (automatic capillary) sequencing machines supplied by Advanced BioSystems (ABI), had transformed the pace of the project. The politics of the moment was to give

equal credit to the private and public sides of the race, *something that in a way was to be repeated and reconfigured on an international scale in China, and in a third way in Singapore.*

One percent of the Human Genome in the short arm of chromosome three was assigned to BGI at the Fifth Strategic Meeting of the International Human Genome Sequencing Consortium at the Sanger Center in Hinxton, U.K., on 1 September 1999 (Liu, Yu, Wang, and Yang 2002: 904). At the time BGI only had two dozen DNA sequencers and inadequate computing, so finding the means of upgrading was critical.

viii Formerly a Postdoctoral Teaching Fellow at Tembusu College, NUS, and now at the Agricultural University of China, Beijing.

ix There are many accounts of this acquisition, e.g.:

<http://www.pehub.com/191692/bgi-shenzhen-acquires-complete-genomics/>;

<http://www.bloomberg.com/news/2012-09-17/bgi-shenzhen-agrees-to-buy-complete-genomics.html>;

<http://www.biospectrumasia.com/biospectrum/news/185483/finally-bgi-shenzhen-acquires-complete-genomics>

x The Wikipedia entry for Yang Huanming (Henry) notes that Wenzhou businessmen (although both Yang and Wang speak of the mayor) helped establish what was then called the Huada Genomics Research Institute, but seems to confuse the fact that Huada is not something separate, but is the Chinese for BGI: Hua (China) + da (big) is the short handle for Huada Jinyin (genome) Yanjiuyan (Institute) as Haiden Chen explained. BGI or Huada has offices in Hangzhou as well as Shenzhen, and does indeed, as the entry says sell services to generate revenue, and is able now to compete for government grants as well as foreign contracts, creating what has been unique structure.

xi After working on a 1% region of the Human Genome, the next step was to try doing the rice genome, particularly the indica hybrid variety used in China and Southeast Asia. An International Consortium was working on japonica, and Syngenta and Monsanto also had rice genome projects, again a struggle between

private and public efforts and modes of innovative competition. Yang Huanming is pleased that BGI's work on the rice genome was immediately put into the public domain. The rice genome proved to be more and more interesting. Although the smallest genome by far of the cereals, it was an order of magnitude larger than the region of the human genome that BGI had cut its teeth on. Although seen as a model organism for monocots, it had quite unusual features that set it apart. And by working on a hybrid, thus having to start with two parental strains, BGI set the ground work for larger comparative genomics analyses of rice strains and for future breeding and engineering of new strains.

^{xii} To facilitate the flow of the story, and avoid unnecessary insertions of "he said" and so on, I adopt the convention of italicizing direct quotations, with my own summaries of portions of the interview in normal type. For the same reason, I do not separate Wang Jian's words out in indented columns as readers tend to segregate or skip those as mere illustrations. The point here is to capture the flow and melody of Wang Jian's infectious enthusiasm and voice and delight in the quirkiness of the story.

^{xiii} One of five machine devices he invented at CalTech that helped revolutionize the field: his protein sequencer, protein synthesizer, DNA sequencer and DNA synthesizer were commercialized by [Applied Biosystems, Inc.](#) and the ink-jet technology was commercialized by [Agilent Technologies](#). In 1992 with financial support from Bill Gates, he moved to the University of Washington and founded the Molecular Biotechnology Department. In 2000 he co-founded the Institute for Systems Biology.

^{xiv} Eric Lander became the head of the genome center at MIT (first at the Whitehead, and then at the Broad Institute).

^{xv} <http://www.biospectrumasia.com/biospectrum/news/159110/consortium-sequence-pediatric-brain-tumors#.UVByxlAv8w>

^{xvi} In August 2013, a third medical school, the Lee Kong Chian School of Medicine a joint collaboration between Nanyang Technical University (NTU) and Imperial College took in its first class of 54 students

(<http://www.lkcmedicine.ntu.edu.sg/NewsnEvents/Pages/Detailed-Page-news.aspx?news=7d989872-0021-4404-b60d-0786edaac952>).