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Pandemic Medicine:
Why the Global Innovation
System Is Broken, and
How We Can Fix It

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1

An Innovation Commons: The Global System for New Drug Discovery

What happened to the global innovation system that makes us—government officials, company executives, patients, and advocates—less prepared than we should be for viral pandemics and such other threats to human health as antibiotic-resistant bacteria and killer parasites? Chronic (noncommunicable) conditions, including asthma, cancer, diabetes, and heart disease, have also risen to epidemic levels. The noblesse oblige of pioneers of modern medicine—the sharing of discoveries in the commons as a communal resource for all humanity—was the norm in the early twentieth century. This open sharing of medical innovations, the introduction of such new goods and services as medicines and treatments to society, was the basis for modern medicine. Prior to the rise of patent-centric intellectual property rights (IPR), novel discoveries had been shared in what can be called an innovation commons.¹ An innovation commons has two key characteristics. First, knowledge flows across institutional and other boundaries, and access is free and open. Second, knowledge and innovation stakeholders often share a sense of civic duty—that is, a sense of responsibility to the community to seek solutions for the common good.

For most of the twentieth century, lifesaving medicines and medical treatments were shared in the innovation commons for the public good. These shared innovations in medicine have included insulin, saving

millions from the debilitating and deadly disease diabetes (1921); the first antibiotic, penicillin (1928); the polio vaccine (1955); and monoclonal antibodies (1975), which have been essential in cancer treatments (Hager 2019).² It is noteworthy that these innovations were all natural biologics—that is, natural medicines derived from living things (e.g., plants, microbes). Unfortunately, the innovation commons of shared discoveries in natural medicine has since morphed into a global juggernaut of drugmakers working with synthetic (i.e., non-natural) chemicals that have intentionally closed off the innovation commons with patent monopolies.³ Patented synthetic chemical drugs have indeed been important in the alleviation of symptoms of chronic conditions and have also been effective in the treatment of infectious disease, although their safety and efficacy had declined by the end of the twentieth century. This innovation decline is examined in Chapter 2.

That is not to say that prior to the twentieth-century (and current) system of monopoly patented drugs, life was idyllic for most. Infectious disease of epidemic and pandemic proportions sickened and killed large swaths of the human population on a regular basis. Certainly, pharmaceutical companies have been effective in producing drugs and vaccines at scale, reaching millions of consumers and patients worldwide. Nevertheless, previous sharing of medicine discoveries in the public commons has been eclipsed by the global race among private companies to dominate markets. Patient health has become subjugated to the drive for profit (Raghupathi and Raghupathi 2018). Human health on the whole has suffered. As a result, the global innovation system for the discovery and development of new medicines is failing to keep up with pandemics and other threats to humanity. To be sure, private actors in international markets are not expected to serve the common good. Nevertheless, when the health of humanity is at stake, incentive mechanisms must be in place to encourage private and state actors to work together in seeking remedies. Such global health crises as pandemic disease expose the failure of private markets to provide opportunities for actors to collaborate in providing social returns on investment. The cost to humanity of this market failure has been catastrophic during the global coronavirus pandemic that began in 2019. The toll has been measured in millions of lives lost, billions of taxpayer dollars spent on pandemic responses that could have been allocated elsewhere, and trillions of dollars in lost economic activity.

In this book I explain how the global innovation system for medicine development became broken in the twentieth century and propose a way to fix it. Absent a complete overthrow of the current patent-centric global intellectual property rights regime—which some argue undermines the potential for disruptive innovation—state and private-sector experiments underway may offer an answer. These include creating spaces of inclusivity in innovation practice that are neither entirely state nor purely private-sector solutions. I call these (innovation) sandboxes and (intellectual property) pools.

Sandboxes and Pools

Transformational change in the way the world innovates for new drug discovery can be explained by innovation sandboxes and shared intellectual property pools within a framework that I call the typology of innovation system architectures (TISA). Sandboxes and pools representing open innovation architectures are situated within the TISA. Innovation sandboxes aim for new discoveries through open exchange within structured play. Examples include transnational collaborative new drug discovery found in India's Open Source Drug Discovery analyzed in Chapter 4. Innovation pools promote sharing between select groups of stakeholders of old knowledge, evident in the competitive collaboration in sharing drug compound libraries for new drug development in Japan's Global Health Innovative Technology Fund (GHIT), explored in Chapter 5. The TISA framework reflects the degree to which interactions aiming for innovation are open or closed and the degree to which the innovation output itself is novel or not. Further, analyzing innovation activity through the framework of the TISA exposes how the current global innovation system architecture for the discovery and development of new medicines has become enclosed into fenced-in spaces. An apt metaphor for this enclosure is a cage, since innovations become trapped and cannot be shared in the commons. These enclosures or cages are secretive, reflecting the efforts of private interests to protect patentable findings from competition. Once caged in, innovation activity tends to become less innovative over time, then stagnates, falling Icarus-like from the novel heights of innovative activity into an enclosure. Closed innovation architectures tend to lead to silos, becoming walled off to

information exchange with the outside (except the one-way extraction of knowledge resources inward). Reliance on old discoveries means that outside ideas that could refresh and renew innovation activities can't get inside. Collectively, innovation cages and innovation silos comprise the anticommons, the opposite of architectures designed to share in the open innovation commons. Figure 1.1 outlines the relationships between open and closed system architectures and the level of market and product novelty. Chapter 2 details and explores the typology of innovation system architectures in light of the rise and decline of innovation in new drug discovery within the global pharmaceutical industry.

As the case studies in subsequent chapters show, removing regulatory barriers is not enough to engender an open innovation commons characterized by sharing of medicine knowledge and resources for the greater good. It is about not only removing the fences and cages enclosing the sandbox of innovative activity but also inviting a greater variety of stakeholders to play in it. Pools of shared medicine knowledge have reduced both transaction costs and redundancy in collaborations for new drug discovery (Nair 2010). In the absence of a global intellectual property rights regime ensuring a global innovation commons, intermediate but nevertheless transformational ways of pursuing innovation for essential medicine discovery and development in sandboxes and pools offer insights into possibilities for the future. Analyzing these trends across countries at the state-private-sector nexus offers a lens on how states and others within the global innovation system have risen to the challenge of promoting innovation for the public good. Findings indicate an offensive strategic nationalism in China, caging in new innovations and preventing them from being shared widely; a global commons, sandbox-guided defensive posture in India; and a middle ground of shared intellectual property pools through international health diplomacy in Japan.

This book is also about the potential for a new, emergent kind of global innovation architecture, presenting successful case study models of new drug discovery and innovation inclusive of certain stakeholders. An inclusive innovation architecture is one structuring incentives for open innovation that benefits (private) firms and (public) states while reducing the burden on national governments and ultimately taxpayers and citizens. This involves improving governance of the global innovation commons (Ostrom 1990), discussed below,

Figure 1.1 Typology of Innovation System Architectures (TISA)

Products and Markets	Closed	Open
High novelty	Cages	Sandboxes
Low novelty	Silos	Pools

while structuring incentives for private-sector actors to act in the interest of human health. This change would help in preparing for future pandemics and also in healing chronic conditions—as opposed to treating their symptoms—through investments in developing novel medicines heretofore neglected by the pharmaceutical industry. The crisis in innovation precipitated by the coronavirus pandemic presented an opportunity to innovate the global innovation system.

Innovation Crisis in the Covid-19 Pandemic

A novel coronavirus erupted in Wuhan, China, in late 2019, spreading rapidly around the world by early 2020. The resulting Covid-19 disease has killed millions and sickened millions more. The pandemic has also disrupted the global innovation status quo. That status quo was one of patents for profit, characterized by private competition to bring drug treatments and vaccines to market. Collaboration under a sense of the general good was all but absent, save existing initiatives by a handful of private foundations.⁴ During the initial response to the coronavirus in early 2020, the global drug discovery and development system was ill prepared, with tragic consequences for human health worldwide. Academic institutions had been conducting pandemic health policy response prior to the coronavirus pandemic, though the United States, for example, at a national level had been retreating from its previous role in funding basic science at universities and public research institutions. The fragmented international response led to an innovation crisis in which national attempts to bring innovative diagnostics, drugs, and therapies to patients were hampered by conflicting national and state policies, as well as different levels of competency in national leadership and international

cooperation. National governments worldwide scrambled to identify and develop diagnostic and vaccine candidates, costing the global economy many trillions of dollars in lost economic activity.⁵ The World Bank (2020) estimated that global GDP shrank in 2020 between 5 and 8 percent due to the Covid-19 pandemic. Initial estimates for 2021 anticipated a drop in global growth by about 1 percent amid ongoing uncertainty (Hannon 2020). In an innovation crisis scenario, actors trade away efficiency in an urgent search of perceived, but untested or unproven, effectiveness.

From the 1990s, the global pharmaceutical product pipeline for drugs and diagnostics had spread across the globe, its “supply chain” stretching from research and development (R&D) centers in cities like Boston and Chicago, to component suppliers in Europe, information technology centers in India, and production that became heavily dependent on mainland China. The world had also become dependent on China for raw biological materials and materials for active pharmaceutical ingredients. While patients were dying in hospitals around the world during the Covid-19 pandemic, the production of test kits was slow as a result of quarantining and the shutdown of the global transportation system. A dismayed epidemiologist noted that the swabs needed for test kits in the United States had been produced almost exclusively in Italy, while Italian researchers with important data and samples had been shut out of their labs, unable to access critically needed information for the pandemic response (*Reset* 2020). Had the intellectual property and tacit know-how been held in an innovation commons, other stakeholders in the research, development, and production of potentially lifesaving drugs and diagnostics could have stepped in to help more quickly and efficiently. Unfortunately, the global innovation commons had become dangerously fragmented, closed behind national and institutional borders—an anticommens.⁶ During the Covid-19 crisis, pharmaceutical firms competed to be the first to market with a vaccine.

In addition to making the unprecedented move of circumventing standard scientific reporting procedures, instead announcing their clinical testing findings in press releases aimed at boosting their stock prices, Pfizer/BioNTech and Moderna told their investors that the companies would be profiting handsomely from the sale of the Covid-19 vaccine, including earning billions of dollars in government vaccine contracts. The first-to-market Covid-19 vaccines bene-

fitted from decades of government-funded research and development, and further, during the pandemic these pharmaceutical companies received cash infusions from public funding to the tune of billions of dollars (Pfizer and Moderna, United States), pounds (AstraZeneca, United Kingdom), and euros (BioNTech, Germany) (Mazzucato, Li, and Torreele 2020; Baker et al. 2020; Hiltzik 2020). Further, Galikina Cleary and colleagues (2018) have noted the role of the US National Institutes of Health in all drugs approved by the Food and Drug Administration between 2010 and 2016 as part of more than \$100 billion in government funds benefiting drugmakers. Political oversight or lack thereof exacerbated the fragmentation and failure to have transparency when clinical subjects became seriously ill from experimental vaccines (Zimmer, Thomas, and Mueller 2020). Part of the reason why there has been so little oversight is the success of the pharmaceutical industry in lobbying governments and multilateral institutions for preferential policies.

The billions of dollars (\$306 billion in 2020 alone) spent by the drug lobby representing the interests of large pharmaceutical companies have resulted in rent seeking in which private-sector actors gain economic benefit from governments without doing the work to earn it.⁷ One example of rent seeking is that these companies continue to earn profits from patents extended on old drugs, called *evergreening*, instead of bringing novel drugs to market. Since 1950, each decade has brought half as many new drugs to approval per each billion dollars spent by the pharmaceutical industry (Scannell et al. 2012). Something about the current architecture for innovation isn't working. A complete replacement of the current system may not be possible, despite the coronavirus crisis. We must, however, innovate our global innovation system for new drug discovery.

Innovation Commons and Human Health

In contrast, the innovation commons approach of the Human Genome Project (HGP) (1990–2003) provided a framework for data and information sharing across national and institutional boundaries. Because the norms and practices of sharing had been in place through the HGP when the severe acute respiratory syndrome (SARS) epidemic struck Asia in 2002, scientists managed to quickly, by early 2003, map the

genomic structure of that virus, enabling effective testing and treatment. This open sharing in the innovation commons—transcending national and particularistic boundaries—helped to avert that epidemic from becoming a pandemic. The disease outbreaks of SARS (2003) and Covid-19 (2020) were both caused by coronaviruses, but in 2020 no HGP-level global collaboration architecture was in place.

The HGP is an example of how a shared goal of identifying gene targets benefited from a structured and committed international effort to bring complementary resources (data analytic technology, scientific talent) to solve common scientific questions. The HGP functioned as an innovation sandbox and intellectual property pool within an open commons framework, on the commons side of the TISA. The origins of the HGP and its impacts have been discussed extensively elsewhere and are beyond the scope of this book (Tripp and Grueber 2011). Briefly, the HGP led to numerous new medical treatments and also to a generation of new venture start-ups in biomedicine, especially in Asian countries (Ibata-Arens 2019a). However promising, the innovation commons approach of the HGP represents an anomaly. Since the 1980s the rules of the global innovation system have been written to encourage profit but discourage open innovation.

The State and the (Pharma) Firm: The Rise of the Global Patent System

To protect the health of their citizens and residents, nation-states play an important role in mitigating negative externalities of global economic competition. Governments thus have a responsibility to maintain a delicate balance between promoting private-sector economic activity (in markets) and engendering innovation that matters to their citizens and humanity (in society). In the early twentieth century, drug companies in the United States and Europe promised to research and develop medicines that improved patient health. In this regard, George W. Merck, in the early years of that eponymous company, was quoted as saying, “Medicines are for the patients . . . for the people . . . not for profit” (J. J. Li 2014). Flash-forward to the 1970s and Merck’s then CEO Henry Gadsden. His interest was more in marketing than in pharmaceutical science. In his own words, changing the script from Merck’s founding motto of “patients before profit,” Gadsden said

that he wanted “to sell drugs to everyone. I want to sell drugs to healthy people. I want drugs to sell like chewing gum” (Robertson 1976; Moynihan and Cassels 2005; see also Hawthorne 2003). Similarly, John McKeen, Pfizer chief executive in the 1950s, argued that it was not worthwhile to invest in drugs that wouldn’t generate wind-fall revenues (Posner 2020; J. J. Li 2014).

Following in the footsteps of McKeen, Edmund Pratt, CEO of Pfizer in the 1980s, headed the coordinated lobbying effort (alongside other multinational corporations with an interest in pharmaceuticals: DuPont, Bristol-Meyers, Johnson & Johnson, and Monsanto) that led to the creation of the patent-centered global intellectual property rights regime under the World Trade Organization (WTO) discussed below (see Drahos 2010; Matthews 2002).⁸ It is interesting to note that the rise of the marketing juggernaut of Pfizer and its sales of drugs on a global scale coincided with Pfizer’s hiring of skilled medical advertiser Arthur M. Sackler. Sackler went on to found Purdue Pharma, whose marketing of the addictive synthetic chemical drug OxyContin contributed to the opioid epidemic in the United States in the 2000s.⁹ Criminal investigations later confirmed that Purdue executives had been well aware that users would likely become dependent on the drug. After all, an addicted user is a repeat customer. Patients might suffer and eventually die, but in the meantime, pharmaceutical company profits would be guaranteed. This is not a new phenomenon.

Pharmaceutical companies grew from early-1900s purveyors of “cure-alls” (Posner 2020), often laced with cocaine or opium. These companies would go on to build a global industry based on broad-spectrum or cure-all antibiotics used in the treatment of bacterial infection, but increasingly as a prophylactic against it.¹⁰ Contagious epidemic disease was soon replaced by noncommunicable chronic disease as the main target for drug discovery in the pharmaceutical industry. Meanwhile, finding it easier to obtain patents granting monopoly sales rights on synthetic chemicals, pharmaceutical companies moved away from developing natural medicines, which had proven more difficult to extract from the global commons unchallenged. Figure 1.2 outlines the different types of drug discovery, showing the variety of material resources within natural medicine discovery and development.

Within the global market share for drugs and medicines—the distinction between “drug” and “medicine” is explained in Chapter 2—medical discoveries based on biologics had accelerated exponentially,

Figure 1.2 Drug Discovery by Type

Natural Biologics
<ul style="list-style-type: none"> • Genomics • Microbes (e.g., for antibiotics)^a • Stem cells • (Re)discovered natural (plant, animal, fungi) chemical compounds from traditional medicine • Vaccines
Synthetic Chemicals

Note: a. Microbes or microorganisms include bacteria, viruses, and fungi (e.g., yeast and mold). Other microbes are algae amoebas and slime molds. Enzymes are not living things but can be produced by microbes, namely, bacteria.

particularly in genomics and stem cell therapies but also in medicines dependent on other biological materials, including those derived from plants and animals. Such synthetic drugs as the first effective HIV/AIDS treatment (azidothymidine, from sea sponges) and blood pressure medications (e.g., angiotensin-converting enzyme [ACE] inhibitors, from the Amazonian pit viper) owe their discoveries to observations of the natural world (Plotkin 2020).¹¹ Unfortunately, synthetic chemical drugs became central to the profits of pharmaceutical companies just as their curative potential was waning.

Medicine and Pandemics: The Need to Save Biological Materials and the Knowledge About Them

By the mid-twentieth century, global pandemics seemed rare, the memories of the 1918 Spanish flu relegated to the pages of history.¹² Then, in 1997, the S5N1 bird flu hit 18 countries, killing half of those who fell ill (estimated 455 deaths). Within a few years, in 2002, the world would battle SARS, which hit a number of Asian countries, including China. Less than a decade later, the 2009–2010 H1N1 swine flu infected 214 countries, killing hundreds of thousands of people. In 2012, Middle Eastern respiratory syndrome spread to 28 countries, killing 858, with a 34 percent death rate. Since 2012, at least five viral outbreaks have

spread around the world, with the novel coronavirus emerging in 2019 to threaten the entire human population. Meanwhile, other diseases endemic to the developing world—malaria, Zika, and dengue fever, to name a few—continue to infect people of all ages, with increasing resistance to the synthetic chemical drugs on the market to treat them (Woodward and Gal 2020; Madhav et al. 2017; Landers and Inada 2020; Chotiner 2020). In sum, the world faces human health crises—including viral pandemics and rampant growth in antibiotic-resistant killer bacteria—that have exposed the curative limits of synthetic chemical compounds sold by pharmaceutical companies.

While on average more people die from chronic conditions, pandemics tend to kill quickly, especially targeting the most vulnerable, the elderly, and those with underlying health conditions. Pandemic diseases result from complex economic, political, and social factors. For example, pathogens are more easily spread among human populations in locations where people interact closely with each other (cities) and among wild and domesticated animals in smaller spaces (Lock and Nguyen 2018; Ackerknecht 2016). Epidemics (illnesses affecting large numbers of people at the same time) and pandemics (epidemics spread across wide geographic space and sickening an unusually high proportion of the population) have been around since the beginning of recorded history.¹³ Why do we seem to be affected by them more now?

Both the number and the severity of viral pandemics are on the rise for the same reasons why the natural medicines with the potential to cure them are about to disappear. Natural medicines depend on biological materials living in biodiverse ecosystems. Urbanization, changes in land use (e.g., monocropping, built infrastructure), and shifts in climate are reducing biodiversity worldwide (Sala, Meyerson, and Parmesan 2009). Shrinking biodiversity is also bringing wild animals into closer contact with human populations. Of the epidemics and pandemics to threaten human health in recent decades (avian flu, SARS, Covid-19, swine flu), evidence points to their pathogens' having jumped from wild animals (bats, birds) to humans (a process called zoonosis), frequently via domesticated animals (chickens, pigs).

Bacteria, viruses, and other microorganisms that cause disease have become more virulent in less biodiverse ecosystems and, further, are more likely to invade human hosts. Cholera, Lyme disease, and malaria are among many examples of human infectious diseases

whose spread worsens within destabilized natural ecosystems (Alves and Rosa 2007). The Covid-19 crisis made clear how humanity depends on biodiversity. Earth's living plants and animals (including microbes) have evolved for millions of years, keeping viral and bacterial pathogens in check within biologically diverse ecosystems (called *reservoirs*). It is in these biodiverse ecosystems that the plant (and animal) genomic resources for medicines reside.

Natural Medicines and the Innovation Commons

Natural medicines have always been an important source of both the quotidian medicine know-how and the biological materials for the development of new medicines. Microbes, for example, are the basis for many vaccines and depend on a biodiverse ecosystem for their survival. Continued availability of and access to these biological materials is dependent on plant biodiversity (cultivated varieties lack the potency of naturally occurring active ingredients), and microbes and fungi need a diverse plant ecosystem to flourish. This medicinal plant biodiversity is under threat from a myriad of factors, some outlined above. Others will be discussed in subsequent chapters in the context of efforts by local organizations to protect and conserve traditional medicine knowledge (TMK) and medicinal plant biodiversity (Center for Biodiversity and Indigenous Knowledge in China, *deo rahati* in India, and Takeda Garden for Medicinal Plant Conservation, Kyoto, in Japan). The emergent organizational case studies from China, India, and Japan offer an opportunity to explore, via grounded theory (Lundvall 2007), how national governments have risen to the challenge—or at least gotten out of the way—of promoting innovation that improves human health while navigating the thicket of rules in the global IPR regime that have prioritized private profit over the public good.

The earth's biodiversity for natural medicine depends on humanity to conserve and protect it. Unfortunately, humanity on the whole has done a poor job of doing so, to the detriment of natural ecosystems that are habitats for wild medicinal plants. Scientists have found that virulent pathogens had previously been held in check by certain microbes and plants in their ecosystems. These microbes and plants have also been critical resources in the development of drugs and

treatments against pandemic disease (Grifo and Rosenthal 1997). Innovations in the discovery and development of healing natural medicines have been made for thousands of years, and these discoveries have been documented extensively in ancient medicine texts. These books of remedies evolved from doctors' notes taken by the bedsides of patients, then evolved in some countries into compendiums of codified medicine formulations. So-called traditional natural medicines are used extensively, for example, in Asian countries, on their own and also in combination with Western methods.

The definition of traditional medicine varies slightly across countries. Generally, the term refers to the holistic practice of medicine, treating a whole person's overall health rather than a narrow (allopathic) focus on a particular disease or condition. Traditional medicines are naturally derived, having no synthetic chemicals. Formulations are inherited and innovated across generations, typically through a master-apprentice training relationship. Formulations of these medicines are routinely innovated, responding to changing patterns in illness, environment, and availability of raw materials. "Traditional" refers to the way knowledge is created, preserved, and transmitted from older to younger—not the knowledge per se. In other words, traditional medicine knowledge is often dynamic and innovative, not static and rarefied (Finetti 2011). TMK stakeholders, including scholars of medicine and traditional medicine doctors, have stewarded and innovated natural medicine knowledge and treatment for thousands of years, maintaining the knowledge corpus in the innovation commons.

The Promise of Biologics: Traditional Medicines and Their (Plant) Biological Materials

As stated above not until the twentieth century did drugs become predominately synthetic chemicals.¹⁴ From the loss of medicinal plant biodiversity follow the decline and loss of potential naturally derived chemical compounds to treat increasing numbers of disease conditions. National governments have borne the bulk of the high-cost burden of emergency treatment and containment. At the same time, growing evidence indicates that such natural medicines as those

derived from wild plant species have significant healing potential (Fung and Wong 2015; Simpson, Sedjo, and Reid 1996; Srinivas 2012).¹⁵ In fact, 85 percent of the world's population depends on plants alone for their primary health care needs (Cox 2009).¹⁶ For instance, ginger (Chang et al. 2013) and ginseng (Im, Kim, and Min 2016) are used as antivirals in medicines made from their rootstalks, called *rhizomes*. Such fungi as mushrooms have been effective in treating bacterial infections (Jakubczyk and Dussart 2020). Other promising innovations in natural medicines are discussed in Chapters 3 to 5. Studies have noted that the greater chemical diversity found in medicinal plants is superior as measured by potency and low toxicity in disease treatment to that in synthetic combinations of chemicals (Fabricant and Farnsworth 2001, cited in Alves and Rosa 2007).

The need to protect, cultivate, and harness natural medicine resources, including medicinal plants and the knowledge about them, for future human health has been recognized by scientists and multilateral organizations, including the World Health Organization (WHO) and the United Nations (Secretariat of the CBD 2005, 2016). Table 1.1 outlines select multilateral policies related to innovations within and protection of natural medicine. Pharmaceutical firms have attempted, with some success, to exploit traditional medicine pharmacopoeia (listing medicines and their formulas and usages) from countries including China and India. Ethnobotanical research methods, combining social scientific study of human communities with observations of the natural world, have been found to be the most effective means of identifying efficacious medicines from the natural world (Cox 2009). For example, the Western field of ethnobotany, which relies on the traditional medicine knowledge of indigenous healers in guiding pharmaceutical research in natural medicine, is said to have originated in the early 1700s with the ethnographic work of Karl Linnaeus. Linnaeus had worked with Sámi healers in northern Lapland, located across the northern provinces of Finland, Norway, and Sweden.

The search for inspirations in new drug discovery has also included data mining of traditional medicine texts and “bioprospecting” for raw materials in such biodiverse countries as China and India (Dalton 2000; Utkarsh 2003; Watal 2000). Critics call this “biopiracy” of indigenous assets and a serious threat to maintaining global biodiversity (Bender 2003; DeGeer 2003; Drahos 2000; Garcia 2007; Ho 2006; Latha 2009; Oyewunmi 2013; Stenton 2003). For

Table 1.1 Key Multilateral Policies Related to Natural Medicines

Year	Policy	Aim	Organization
1993	UN Convention on Biological Diversity (CBD)	Promote conservation and sustainability of biological diversity and seek fair and equitable benefits sharing in genetic resources (Convention on Biological Diversity 2020b)	UN CBD
1995	Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS)	Institute a comprehensive, multilateral legal agreement on intellectual property (WTO 2020)	WTO
2000	WHO Traditional Medicine Strategy 2002–2005	Outline WHO’s role and strategy for traditional medicine in health care systems (WHO 2002)	WHO
2001	Doha Declaration on the TRIPS Agreement and Public Health	Reaffirm right of WTO members under the TRIPS Agreement in order to protect public health and enhance access to medicines (WHO 2020b)	WTO
2003	Cartagena Protocol on Biosafety	Ensure biosafety from potential risks of handling, transporting, and using living modified organisms (Convention on Biological Diversity 2020a)	UN CBD
2008	Global Strategy and Plan of Action on Public Health, Innovation and Intellectual Property	Promote new thinking on innovation and access to medicines (WHO 2020e)	WHO
2009	WHO Traditional Medicine Strategy 2014–2023	Help member states to develop and implement policies and plans to strengthen the role of traditional medicine in health care systems (WHO 2013)	WHO
2010	Strategic Plan for Biodiversity 2011–2020	Promote the implementation of the objectives of the CBD (Convention on Biological Diversity 2020e)	UN CBD
2011	WIPO Re:Search	Support early-stage research and development against neglected tropical diseases, malaria, and tuberculosis (WIPO 2020)	WIPO
2014	Nagoya Protocol on Access and Benefit Sharing	Promote benefit sharing of genetic resources in a fair and equitable way (Convention on Biological Diversity 2020c)	UN CBD
2018	The Nagoya–Kuala Lumpur Supplementary Protocol on Liability and Redress to the Cartagena Protocol on Biosafety	Provide international rules and procedures in the field of liability to promote objectives of the CBD (Convention on Biological Diversity 2020d)	UN CBD

Note: World Health Organization (WHO), World Intellectual Property Organization (WIPO), and World Trade Organization (WTO).

millennia, natural medicines have been integral to human health in these societies, and, further, research and development into medicines has been shared in the public commons.

Consequently, knowledge about and innovations in these ancient traditional medicines have been maintained in an innovation commons, transcending national and institutional boundaries. Traditional medicine knowledge encompasses the theories and practice of medicine concerned with caring for holistic human health (the overall health of a person) and the prevention, diagnosis, treatment, and cure of illness. It is often contrasted with “modern” or “Western” medicine in that the latter tends to focus on treatment of disease after a person has already become sick. Traditional medicine is also called natural medicine as it avoids the use of synthetic chemicals and focuses on the body’s natural immune response in the treatment of disease. The origins of natural medicine predate Western medicine by thousands of years and therefore focus on natural nonsynthetic chemical medicines. In the span of human history, synthetic chemical drugs are a relatively recent phenomenon in treating illness.

As discussed below, a handful of drug manufacturers—synthetic chemical pharmaceutical companies together called Big Pharma (so named due to their market dominance, high profits, and political influence)—have captured the global market for medicines. Part of this market capture has included creating a global intellectual property rights regime supposedly promoting innovation, arguing that without many decades of monopoly protections on patented drugs, investments into developing new medicines would not otherwise occur. Unable to patent nature, though not for want of trying, companies have opted to alter and manipulate naturally occurring chemical compounds into synthetic chemical drugs. The easiest way to copy natural chemical active ingredients is by observing how natural medicines have been used in treating patients, either directly or via referencing ancient medicinal texts. Also common has been the extraction of requisite biological materials from their natural ecosystems while bypassing stewards of the sustainable use of these materials. In the biological material extraction process, exploiting youth in poor rural communities has been problematic in India, as discussed in Chapter 4. For example, bioprospectors, in their search for biomaterials, typically pay local youth who might know the location of wild medicinal plants but lack the training to harvest sustainably

or knowledge about why these materials are important community assets to be protected from unfair outside exploitation. Historical victims of this exploitation of resources in the commons include vast tracts of wild plants and ocean animals worldwide (Aoki 1998). More recently, in 2020, during the race to develop a Covid-19 vaccine, the world's population of sharks was threatened in the search for the adjuvant squalene, which stimulates immune response. Squalene is abundant in shark livers (Meneguzzi 2020).¹⁷ As analyzed in the chapters that follow, rather than being protected and conserved, natural medicine knowledge and material resources have been extracted from the commons and used with impunity by Big Pharma.¹⁸ The drive to maintain monopoly patents is behind this exploitation.

Patents in Perpetuity

The global market has failed to keep the innovation commons open and inclusive of knowledge stakeholders or to invest in the development of curative medicines. That the global pharmaceutical industry, as of this writing, on average invests 75 percent of research and development into miniscule, literally molecular-level, incremental changes to existing synthetic drugs exposes the fact that the current global innovation system is producing very little radical innovation in medicines, leading to stagnation. Instead, pharmaceutical companies are focusing on obtaining patents in perpetuity for drugs developed decades ago, themselves thanks ultimately to natural medicine and original sharing of discoveries about biologics in the innovation commons. In sum, under the pressure of market competition, unless they can patent it for profit, companies lack incentive to bring discoveries to society. With the increasing potential of biologics, we are in urgent need of innovation system reform, since ceding power over life itself by allowing nature to be patented would have dire consequences for the (plant medicinal) biodiversity of this planet and consequently for humanity. As Drahos (1999) has put it, “The scope of patentability is expanding while the role of moral standards in the operation of the patent system is being increasingly limited.”

At the same time, poor and low-income households either cannot afford and/or lack access to Western mass-produced synthetic drugs, and persistent commodification of traditional herbal remedies puts

upward pressure on prices and has led to overharvesting of medicinal plants. The future biodiversity of the earth from which healing medicines can be derived, therefore the stability of human health, is at stake. A number of investigative journalistic publications have exposed how so-called Big Bad Pharma uses its powerful political influence on national governments' foreign economic policies as well as within multilateral organizations like the World Trade Organization. In other words, powerful corporate interests use these fora to set the rules of the innovation game in their favor (Posner 2020). In this regard, the WTO became the arbiter of who gets to claim monopoly profit rights over innovation outputs. This has been in effect since the mid-1990s, as discussed below.

In response to market failure, national governments, especially in the developing world, face the dual challenges of supporting biopharmaceutical research and development to discover healing remedies and at the same time protecting national assets, including biodiversity in plant and other biological materials (Boldrin and Levine 2009). These challenges transcend national borders and have led countries to seek transnational and multilateral solutions—often in direct response to the capture of the WTO by Big Pharma.

For example, the voice of stakeholders in developing countries was excluded from the design of the WTO Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS), discussed in detail in Chapter 2. The TRIPS fused international trade (i.e., access to US and European markets) to an IPR regime reifying exclusionary patents.¹⁹

In response, a transnational effort, led by nonprofits, community health organizations, and national governments representing developing countries in the Global South, led to amendments to the TRIPS allowing flexibilities in compliance with the agreement so that at-risk communities could access essential medicines at affordable prices.²⁰ Essential medicines are those necessary for basic health care needs of the population—for example, antibiotics and vaccines (WHO 2020c).²¹ The movement also led to the establishment of public-private partnerships (PPPs) for essential medicine drug discovery and development. For example, the Medicine Patent Pool under the World Health Organization is one such PPP. TMK stakeholders have also turned to the United Nations.

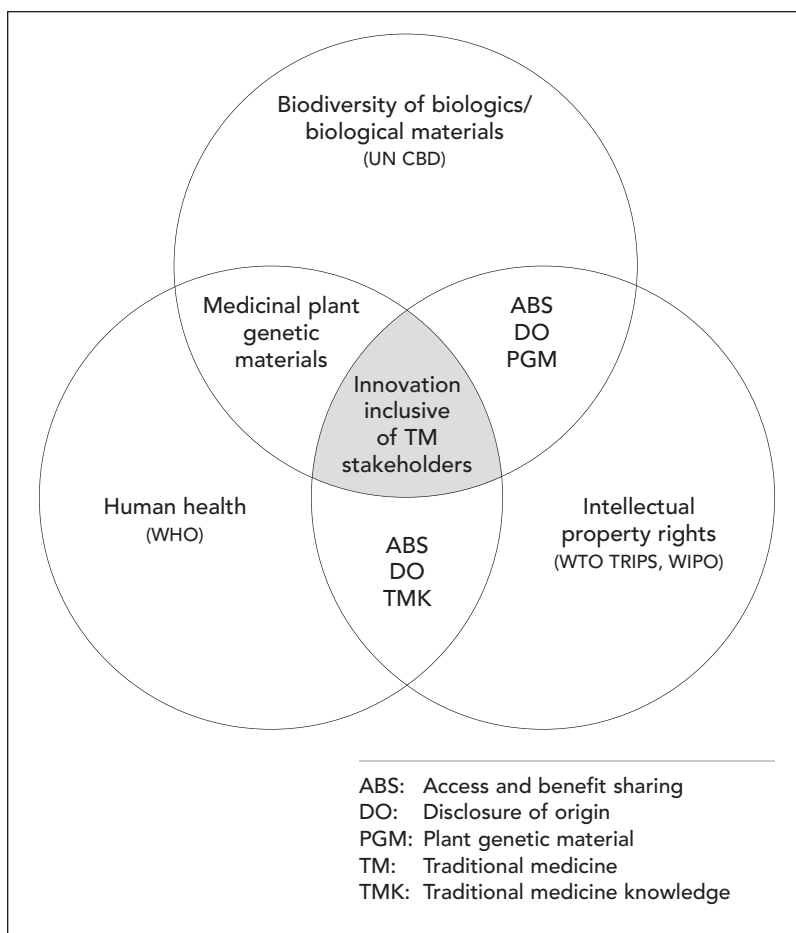
Under the UN Convention on Biological Diversity (1993), pharmaceutical companies would have to disclose the origin of the plant

genetic materials of compounds extracted from nature and natural medicines, while acknowledging the contributions of traditional medicine knowledge stakeholders. Efforts within the World Intellectual Property Organization have also been attempted. Unfortunately, without the carrot and stick of market access or exclusion afforded by the WTO, these efforts have had limited impact in stimulating investments into drug discovery inclusive of natural medicines and their stakeholders. Consequently, the global IPR regime resides *de facto* within the WTO under TRIPS (Sengupta 2019).

The global innovation system has thus become fragmented into issue areas controlled by multilateral organizations each claiming domain. These supranational organizations purportedly represent the interests of all nation-states and thus humanity writ large. Some have argued that the WTO in particular instead protects the vested interests of a small number of multilateral corporations (Drahoš 2010; Matthews 2002). As discussed below, the study of innovation that is inclusive of the needs of human health transcends disciplinary boundaries. For example, national and multilateral politics and policy often guide and regulate the global system governing new drug discovery. Likewise, access to knowledge about natural medicines depends on the protection and conservation of TMK and plant medicinal biodiversity. Further, as the knowledge about traditional medicines is lost (discussed in Chapters 3 and 4), so is resistance to unsustainable use of plant medicinal materials. Figure 1.3 illustrates these disciplinary intersections and overlapping issue areas.

The current structure of the global innovation system reflects the increasing power of patent-centric IPR as governed by the WTO TRIPS. Meanwhile, we are witnessing a steady creep of patents further into the natural world. Namely, patents have been granted for biologics, extracting them from the public commons of material natural resources. This extraction benefits pharmaceutical companies mostly while neglecting overall human health.²² As outlined in Figure 1.3, the complexity of the challenge of creating spaces for inclusive innovation is evident in the interconnectedness between policies governing the protection and conservation of medicinal plant biodiversity, access and benefit sharing in intellectual property rights, and the development of essential (natural) medicines for better human health. This study is at the center of the overlapping issue areas of biodiversity, human health, and intellectual property rights in a global context. For

**Figure 1.3 Natural Medicines in the Innovation Commons:
Issue Areas (multilateral organization domain)**



example, biodiversity-related issues include such genetic materials as medicinal plants. The boundary-spanning issues of concern also relate to intellectual property rights in terms of who gets enriched at the expense of whom within a patent-centric global innovation system governed by IPR within the WTO TRIPS system.

In a November 2020 open letter to the WTO TRIPS Council, a transnational network of sixty-seven scientists, politicians, scholars, and activists called on the WTO member states to approve a waiver to TRIPS, granting permission to developing countries to access the patented vaccines at fair and equitable prices. Further, they called

upon pharmaceutical firms to share the tacit know-how to produce Covid-19 vaccines and other critically needed Covid-19 diagnostics. Without this waiver, millions of people would die unnecessarily from Covid-19 (Baker et al. 2020). As of May 2021 lobbyists representing Pfizer and other pharmaceutical firms continued to block these appeals in the WTO (Fang 2021).

Among the key findings of the 2019 Global Innovation Index (Dutta, Lanvin, and Wunsch-Vincent 2019) was the need for more investment into medical innovation for health, as well as greater diffusion of existing innovations. The report further noted that while medical innovations were critical in reducing disparities in who gets access to health care on a global level, pharmaceutical research and development had continued to decline (Dutta, Lanvin, and Wunsch-Vincent 2019). Meanwhile, China had become the most prolific patentor in pharmaceuticals. The United States, China, and Japan led in biotechnology patent publications. At the same time India grew increasingly specialized in pharmaceuticals relative to other kinds of patents within its domestic innovation system.²³ The report speculated that the decline in medical innovations, despite the rising need for them, might reflect “fundamental structural problems within the biomedical innovation system and incentives facing public and private sector researchers” (Dutta, Lanvin, and Wunsch-Vincent 2019). In other words, the global structure for innovation had broken; it was not just a market failure but a global system failure.

Innovation Systems

An innovation system is comprised of the institutions and people creating and producing new goods and services for society and markets. Healthy innovation systems have certain features—for example, a capacity to generate new ideas. This activity should be self-sustaining over time. New ideas in the innovation system for drug discovery and development ideally contribute to improving quality of life, stimulating new investment, encouraging a healthy, stable workforce, and improving quality standards in new drug development.²⁴ Institutions within innovation systems include the rule of law, regulations, government policies, and so forth. Institutions and practices within healthy innovation systems operate at various levels: local, regional, national, transnational, and global. Healthy innovation systems are open to tacit

knowledge exchange, learning by doing, and other ways in which knowledge is shared in an open and inclusive innovation commons. An innovation architecture is how structures cohere together and function to support innovation activities. For example, the nation-state has autonomy to make innovation policy decisions within domestic economies. States are limited by competition from other states within the international system as well as constrained by supranational organizations, including the WTO, as mentioned previously.

Underexamined is how public- and private-sector actors, through collaborative spaces in emergent organizations (emergent in the sense that they are unique and not a copy of preexisting forms), some of them PPPs while others are more loosely networked, have sought to innovate our global innovation system for new drug (re)discovery. Leading transformative change in the global innovation system, thus improving innovation outcomes that serve human health, has been a priority for a variety of global actors. These include transnational networks of civic-minded actors through best-practice innovation architectures. PPPs, defined in detail in Chapter 2, are providing powerful lessons. These lessons are explored in historical-institutional detail in Chapters 3 (China), 4 (India), and 5 (Japan).

Research has found that certain transnational actors—those that have ample financial and human capital resources and also normative influence, for example, through their humanitarian vision—might be a basis for transformational change at the global level (Binz and Truffer 2017). It is at this intersection of the structures within the global political economy and the agency of individual national and transnational organizations that the study of inclusive innovation resides. That is, individuals and organizations pursuing innovation activity inclusive of human health and humanity in both outcome (who benefits) and process (who gets to participate) must navigate system-level rules and often powerful entrenched interests bent on maintaining exclusionary structures. Exclusionary practices are evident in the building of enclosures around innovation activities, the TISA anticommmons outlined above. This includes Big Pharma attempts to patent nature, thereby fragmenting the global innovation commons. This behavior is not new.

Beginning in seventeenth-century England, privatization of land that had been underway for centuries was codified by Parliament in a series of “Enclosure Acts.” Traditional rights to access lands shared in the commons for grazing animals were eliminated.²⁵ The

enclosure of such modern intellectual property rights as codified in patents and copyrights is likewise the closing off of a resource from sharing within a public commons (Yu 2007; Boyle 2003; Runge and Defrancesco 2006).

Enclosure attempts are evident under the original version of the WTO TRIPS. Savvy business executives know that influencing the global standard setting—in other words, the rules of the game—of innovation is an effective way to ensure the longevity of their products and their sales revenues in global markets (e.g., through drug patent “evergreening”). Under the WTO TRIPS, for example, companies and countries unable or unwilling to comply with the patent monopolies on high-priced drugs and antibiotics can be excluded from exporting their goods and services to WTO member markets.²⁶ The WTO markets together make up most of the global economy. Ideally, the world needs a *sui generis* global innovation system comprised of an innovation commons for essential medicines.²⁷ Realistically, possible in the near term are meso-level improvements, including the inclusive innovation approach (sandboxes and pools within the TISA commons) exemplified by case studies of emergent organizations, including certain PPPs, analyzed herein. At the same time, the coronavirus pandemic has created an interstice of opportunity in the emergence of alternative ways of thinking about and doing innovation, which the emergent organizations analyzed herein exemplify. As such, their impact might prove closer to a Schumpeterian gale of creative destruction rather than leaving the system as is, in a state of innovation decline, by continuing to prop up the institutions of the status quo (Schumpeter 2005 [1942]). In other words, these emergent actors have become agents of change for the global structure of innovation. How are ideas about system transformation and actions to make it happen related?

First, the lens of emergent organizations, including PPPs in new drug discovery for natural medicines (biologics), is a way to reflect on the state of the field of the study of innovation in global context. Second, it shows the challenges nation-states and domestic actors are facing in succeeding, but sometimes failing, in the pursuit of innovation that matters for human health. The emergent organizations analyzed in subsequent chapters are focused on developing and rediscovering biologics that show promise to cure a range of diseases and conditions. It need not be mentioned that synthetic chemical drugs, comprising the vast majority of drugs on the market and in the R&D

pipeline of global pharma, have not lived up to the promises made by industry lobbyists.²⁸ Data on this is outlined in Chapter 2.

Toward an Open Architecture of Innovation

Since the twentieth-century rise of the global pharmaceutical industry, we have been conducting innovation for new drug discovery in separate, fenced-off spaces, the cages and silos of the TISA. Efforts to include local TMK stakeholders, for example, in bioprospecting for (new) natural drug compounds, have had a spotty track record. In the 1990s Costa Rica's national government was a first mover in this regard, bringing in Merck Pharma to bioprospect for natural chemical compounds in its biodiverse rainforest (Hammond 2015). Initially, the partnership received positive reviews in international media. After a time, it was found that the local stakeholders who were supposed to benefit had been excluded (Grifo and Rosenthal 1997). Within a decade, the project had collapsed. Observers speculated that the availability of substitute sources of biodiverse bio assets in other countries made the costs of Costa Rica's arrangement unattractive (Simpson 2019). Likewise, the US start-up Shaman Pharmaceutical and the WTO/WHO InBio had both gone defunct within a few years after launching, reflecting the difficulty of making local stakeholder inclusion economically viable. These high-profile failures make even more noteworthy the emergent inclusive innovation architectures in place within the case studies in natural medicine and new drug discovery analyzed in this book.

Multilateral (WTO, UN, WHO) and multinational (corporate social responsibility) activities often receive the most international press attention. Meanwhile, emerging transnational actors and networks—for example, those with global reach, including such partners as the Bill & Melinda Gates Foundation and the Wellcome Trust—may be having important impacts, without fanfare on the ground, with local communities in capacity and resilience building, establishing network synergies that lead over time to sustainable economic practices and even democratization, going beyond popularized “ecosystem services”²⁹ and the like. These and other philanthropies have held “grand challenges” to incentivize research and development into essential medicines. Similar efforts by other grassroots

and transnational actors, illustrated by the case studies of inclusive innovation in the chapters that follow, provide insight into the local and global dynamics of stakeholder inclusion that is more than distributive in outcome.

Since so many of the most impactful discoveries of medicine were made by accident (e.g., penicillin), usually by bringing some outside knowledge, experience, or person to the project—a sandbox, not a silo—it follows that for a new generation of drugs and medicines, it makes sense to provide incentives to set various different talented minds to the tasks and to related activities from which novel, serendipitous discoveries can occur. In sum, the inclusion of diverse stakeholders in the innovation process can lead to new discoveries. Including more people in innovation sandbox activities is a first step.

The second way to coax players within the global innovation system into sharing a bit more in the innovation commons is creating shared pools of patented and proprietary libraries of compounds.³⁰ Japan's Global Health Innovative Technology Fund, discussed in Chapter 5, is a recent example of how to do this. Briefly, GHIT is a PPP backed by leading Japanese pharmaceutical firms in partnership with government ministries. GHIT researchers benefit from access to shared pools of heretofore underutilized and off-patent compounds. Participating researchers from around the world can access these resources in new drug discovery research and development. GHIT is focused on bringing new drugs and diagnostics to the developing world to treat endemic diseases, called neglected tropical diseases because they have attracted little attention from major pharmaceutical companies. They are “neglected” by Big Pharma because discovering treatments and cures for these diseases is unlikely to reap significant, if any, return on investment. The noblesse oblige of the global pharmaceutical industry died long ago, if it ever existed at all. Major multinational companies are discovering, however, that doing good actually does, in some cases, lead to doing well as first movers (see CIPLA in Chapter 4 and Takeda Pharmaceutical in Chapter 5). In other words, the right kinds of corporate social responsibility have on occasion led to serendipitous discoveries and thus improvements to the bottom line of profits (Falck and Hebllich 2007; Preuss 2011).

An innovation boom in biopharmaceuticals has been underway in Asia as that region continues to grow into the center of the global economy (Baur et al. 2019). The empirical case studies focus on China,

India, and Japan for two reasons. First, China and India are both megabiodiverse and have among the world's oldest documented histories of traditional medicine practice and scholarship, drawing from vast national natural medicine biological resources and deep medical knowledge. Second, despite these similarities, they have varied in their policies toward incorporation of their ample natural medicine expertise and plant genomic resources into modern drug discovery. Both China and India have launched new drug discovery policies incorporating TMK into R&D domestically and health diplomacy internationally. However, they have differed substantially in their approach to protection and conservation of the tacit knowledge and biological materials for natural medicine. Japan's small geographical size in comparison makes it resource dependent. Nevertheless, it also has a long lineage of traditional medicine. Its *kampo* (literally "Chinese drug") medicines depend almost entirely on plant materials from China. Japan's policy responses have thus been very different from those of China and India.

The TISA innovation sandboxes and resource pools outlined above in the context of discoveries in biologics have proven their viability on a limited scale, as evidenced by the case studies in the chapters that follow. Tackling the challenges involved in protecting and conserving the earth's living system biodiversity is beyond the scope of this book. Nevertheless, on a more limited scale, this book also explores ways in which local communities have partnered with national governments, supported by private foundations and firms, in collaboration with multilateral organizations to save our planet's critical natural plant medicinal resources for future generations of drug discovery. Before outlining the chapters in this book, I will provide a brief overview of the methods employed in this research.

Methods

The methods of this research include historical-institutional analysis of policies supporting open and inclusive innovation in new drug discovery, complemented by original case studies in Asia. Semi-structured interviews were conducted from 2016 to 2020 with government officials, representatives of non- and quasi-governmental organizations and foundations, entrepreneurs, and investors. I also engaged in par-

ticipant observation at policy-related meetings, with PPPs, and in local community organizations, as well as with traditional medicine practitioners and inside medical clinics.

Interviews with local stakeholders, including natural and traditional medicine doctors, nonprofit organization founders, funders, community activists, government officials, and so forth, were conducted in the national languages of each country (directly by me in Japan; aided by interpreters and document translators in China and on occasion in India), supplemented with secondary sources including archival research (e.g., held by international foundations and in local repositories).³¹ Limits of the analysis include lack of familiarity with indigenous dialects and languages of China and India, which would surely have added greater depth to the analysis. Other limitations include the absence of national-level, publicly available aggregate data on the total number of similar TMK-biodiversity-focused organizations, projects, and network activities, as well as a lack of standardized reporting of statistics of funds expended at regional and local levels on these activities, numbers of personnel involved, and to what degree this reflects national-level interest in these matters.³² Nevertheless, local stakeholder perspectives are integral to the pursuit of effective policy and practice that is more substance than statement. This book attempts to fill some of these conceptual and empirical gaps.

Chapter Previews

Chapter 2 reviews the rise and fall of innovation in the pharmaceutical industry with reference to prior attempts at explaining how the current structure of global innovation came to exist and has since faltered in producing novel innovations. It then outlines the TISA framework to analyze innovation systems by their architecture (the way they are structured) and their contributions to developing new, novel products, including drugs and medicines. Subsequent chapters provide empirical context to apply the inclusive TISA innovation sandboxes and pools framework on the ground, evident within emergent organizations, in collaboration and sometimes conflict with the state.

The empirical chapters present organizational case studies of inclusive innovation in China, India, and Japan as a lens to analyze national-level policies contextualized within the global innovation

system. Doing so provides a way to analyze, in a limited empirical context, nested levels of innovation—local, regional, national, and international—within a global system of innovation while at the same time transcending national and institutional boundaries. Chapters 3 to 5 (country-level empirical case studies) have the following layout. First, the chapters begin with a brief overview of the historical interrelationships between natural (or “traditional”) medicine and modern medicine discovery and development. I have written extensively elsewhere about the role of the national government in stimulating innovation in modern pharmaceuticals (Ibata-Arens 2019a). Here the focus is on the innovation (and pandemic preparation) potential of incorporating biologics, including traditional medicinal stakeholders and stewards of medicinal plant biodiversity, into drug (re)discovery and development. Second, each chapter outlines how the state and private-sector actors have dealt with protection and conservation of medicinal plant biodiversity—and essential knowledge about it—for the purpose of maintaining plant genetic diversity in material resources for drug development and discovery. Third, through fieldwork-based original case study analysis, the role of innovation sandboxes and pools in structuring inclusive innovation practices is analyzed. Particular focus is on how local efforts have benefited from engagement internationally, including with transnational-boundary-spanning actors connecting stakeholders with multilateral organizations and multinational corporations. The chapters conclude with possibilities for the future of inclusive innovation in and by the subject country. As such, a TISA analytical lens represents a meso-level step toward or foundation for reestablishing a global innovation commons for essential medicines.

The chapters that follow focus on looking forward in identifying and analyzing promising new intersections of people and institutions seeking transformative change in the way we innovate. Chapter 2 offers a glimpse back to how we got here, reviewing explanations for why we find ourselves in this situation of market and innovation failure in the face of a global pandemic. The past is important for understanding our present, and learning from it is a step toward transformative change within institutions and calls to action to innovate for what truly matters for human health and by extension humanity.³³

It might be that in looking forward we will see the possibilities for new innovation architectures or *sui generis* regimes that are nei-

ther purely private markets nor entirely public entities. What are the best practices in stimulating sustainable innovation in essential medicines? The cases analyzed herein reflect on three distinct approaches: working within the current system (accepting the structure as is) of prizes and grand challenges; proposals, as change agents, for a return to a global innovation commons or the creation of other *sui generis* systems; and something in between, a hybrid emergent organizational experiment evident in certain PPPs. Is it possible that hybrid organizational forms (emergent kinds of PPPs) between markets and states are the best option moving forward? Further, what is the role of such transnational actors as foundations, philanthropists, and nongovernmental organizations in facilitating these emergent processes? Analysis of the innovative organizational forms in Chapters 3, 4, and 5, followed by a call to action in Chapter 6, are helped by a look back in Chapter 2 to the rise and fall of innovation in twentieth-century drug development—namely, the global pharmaceutical industry and its relation to systems of innovation. The story begins with drugs.

Notes

1. The word *patent* derives from the Latin *patere* (“to lay open”), referring to a letter from a monarch granting some exclusive right. A letter of patent would be made available for the public to view.

2. Insulin was discovered by three scientists who donated their patent to the University of Toronto (selling their stake for \$1 each for a total of \$3). Eli Lilly repatented insulin in the United States (see Thompson 2018).

3. Pharmaceutical companies have also attempted to patent nature for monopoly profit, as will be discussed below.

4. A number of international collaborations were established to jointly develop treatments and/or vaccines for the coronavirus in 2020. Incentive mechanisms proposed to stimulate investments in vaccine development included megafunds, which were supranational to distribute investment risk (Vu et al. 2020). Other efforts included procurement (guarantees to purchase vaccines produced) (Paun 2020).

5. Not to mention defection from multilateral collaborations, exemplified by the United States’ defunding of the WHO in 2020 (BBC 2020).

6. Anonymous sources in pharmaceutical companies confirm that given the race to patent and commercialize synthetic chemical drugs, the industry culture is one of secrecy (anonymous interviews 2018, 2019).

7. According to OpenSecrets.org, in 2020 the pharmaceutical industry spent more than \$306 million lobbying US government officials. See “Pharmaceuticals/Health Products, Industry Profile: Lobbying, 2020, Graph, Annual Lobbying on Pharm/Health Prod, Total for Pharmaceuticals/Health

Products” (OpenSecrets.org 2021). Totals included \$306,226,988 spent on behalf of 467 clients, represented by 1,502 lobbyists.

8. Historians have noted the role that patent agents, in their own pursuit of profit, had in persuading drugmakers to focus on obtaining patents (see also Moser 2013).

9. The differences between founding and successor generations of pharmaceutical industry leaders reflect the shift in innovation for medicines from a focus on patients to one that puts patient health secondary to profits.

10. The spread of antibiotic-resistant killer bacteria (e.g., methicillin-resistant staphylococcus aureus) was in part a result of the improper use and overuse of broad-spectrum antibiotics.

11. ACE inhibitors lower blood pressure by relaxing veins and arteries.

12. The Spanish flu of 1918–1919 killed up to 50 million people; in comparison, the viral disease HIV/AIDS, which has yet to have a vaccine, has killed up to 35 million since its outbreak in 1981 (LePan 2020).

13. One could say that pandemic disease has always afflicted human populations, intensifying with the movement of peoples across space, especially along trade routes (LePan 2020). The black death of the fourteenth century, a bacterial pandemic spread via rats and fleas, is estimated to have killed more than 200 million people, possibly 50 percent of the entire population of Europe at the time (Berezow 2014).

14. Synthetic drugs ingested by humans make their way into the water supply via sewage systems, with detrimental effects on wildlife.

15. For example, during the SARS1 pandemic (2002–2003) in China, Guangdong province was found to have the lowest mortality rate due to its reliance on traditional Chinese medicine-based treatment of patients.

16. Natural biologic medicines also include those derived from animals and microbes, as defined below.

17. Indicating the interest in the study of sustainable resource management of the commons, the *International Journal of the Commons* has published a number of articles on the subject (e.g., Lucchi 2013).

18. See Hoareau and DaSilva (1999) for a review of the use of medicinal plants in the pharmaceutical industry (Mgbeoji 2014).

19. See Boldrin and Levine (2008) for a discussion of IPR as stifling innovation and creativity.

20. See Karl Polanyi, *The Great Transformation*, for a historical-institutional analysis of societal response to state and market failure in times of crisis and volatility.

21. The WHO maintains a list of essential medicines.

22. For an overview of institutions involved in the governance of global health, see Harman (2012).

23. See Table T-1.1 in the 2019 Global Innovation Index for an overview of the top origins of health patent publications between the years 2010 and 2017 (Dutta, Lanvin, and Wunsch-Vincent 2019).

24. It need not be said that healthy workers are productive workers.

25. See “Enclosures,” chap. 3 in Polanyi (1944).

26. Defenders of the TRIPS have argued that there was always economic disparity in who gets access to essential medicines and that the TRIPS system did not worsen it (Khair 2016).

27. Brown and Susskind (2020) discuss public health in the context of the Covid-19 pandemic as a global public good, or “GPG,” that should be provided for through international cooperation.

28. Annually in the United States alone, the pharmaceutical industry spends more money on influencing politics in Washington, DC, and by extension Geneva, the seat of the WTO, than any other industry. Pfizer has been at the top of the list in this regard, spending more than \$4 billion since 1998 (Frankenfield 2020).

29. So-called ecosystem services have been a way to incorporate the protection and conservation of the earth’s biodiversity into liberal economic discourse—for example, how having a biodiverse ecosystem “services” our access to clean water.

30. Thaler and Sunstein (2008) refer to this as “nudging” (see also Thaler and Sunstein 2003).

31. Scholars of traditional medicine and the history of medicine have been instrumental in tracing the lineage of ancient, premodern, and modern medicine (see, for example, Ackerknecht 2016).

32. In most Western medical systems, traditional medicine is often referred to as alternative or complementary medicine, thus implying that Western medicine is the standard around which traditional medicine varies or that it supplements. As discussed in subsequent chapters, the definitions of traditional versus modern are more comprehensive in Asian countries.

33. For example, there is no doubt that Asian countries’ experience with colonialism profoundly affected developmental innovations and trajectories, but this is beyond the scope of this book.