Patents

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Drug licensing as evidence of evolution, diffusion and catch-up in East Asia

Data-driven results map a holistic landscape of drug licensing and biotechnology diffusion in the last two decades.

Based primarily on examples from the energy and technology sectors, previous studies have identified a 'linear' route of knowledge diffusion and technological catch-up in East Asia, that is, from the United States to Japan, to South Korea, to Taiwan and mainland China[1–3]. However, the universality and generality of this route in other sectors remains unverified, particularly in a newly emerged sector like biopharmaceuticals. Fortunately, the explosive growth of in-license/out-license projects in the last two decades (2003–2022) provides us with many examples with which to situate this aspect of the biotechnology and pharmaceutical sectors[4–6]. With 5,433 original records in the MarketLine Advantage database, we developed a systematic approach to identify the geographical distributions and spatial networks of drug licensing. For some licensing projects, geographic locations or spatial networks could not be clearly identified because of a lack of related information disclosed. In addition, the targeted regions of some licensing projects are (nearly) global, with minimal meaning for showing knowledge diffusion and technology transfer. Removing these, we selected 3,058 projects as valid data to support further analysis. The initial outcome gives a holistic perspective on the heterogeneous roles and changeable focuses of licensing projects in East Asia.

Overall landscape

Drugs in-licensed in East Asia mainly come from the Asia-Pacific region (61.9%), followed by North, Central and South America (21.8%) and Europe, the Middle East and Africa (16.3%). At a finer-grained level (Fig. 1a), Japan contributes the most (24.8%), followed by the United States (20.7%), mainland China (19.3%), South Korea (11.3%), Switzerland (2.7%), the United Kingdom (2.1%) and Taiwan (2.1%).

While the Americas out-license more projects to East Asia, their East Asian project count as a percentage of their total worldwide is lower than that of the Europe, Middle East and Africa region (Americas, 7.7%; Europe, the Middle East and Africa, 21.8%; Asia-Pacific, 43.8%). This is caused by the different roles of overseas expansion and transnational licensing: mature multinational corporations with established overseas arms may prefer to launch new biopharmaceutical products by themselves. Therefore, the percentage of Americas East Asian licensing projects gradually decreases with the establishment of American corporations' subsidiaries in East Asia (Fig. 1b), whereas most medium-sized and small European corporations tend to collaborate with local corporations in Asia through licensing projects.

Spatial evolution

We see a trend in spatial evolution if we classify these licensing projects according to their start times. In the 2000s, Japan and South Korea were the major targets of licensing projects to East Asia. But in the last ten years, the number of licensing projects targeting mainland China has experienced stable growth. This trend has been especially clear since 2015 (Fig. 2): the percentages of licensing projects in Japan, South Korea and Taiwan has generally

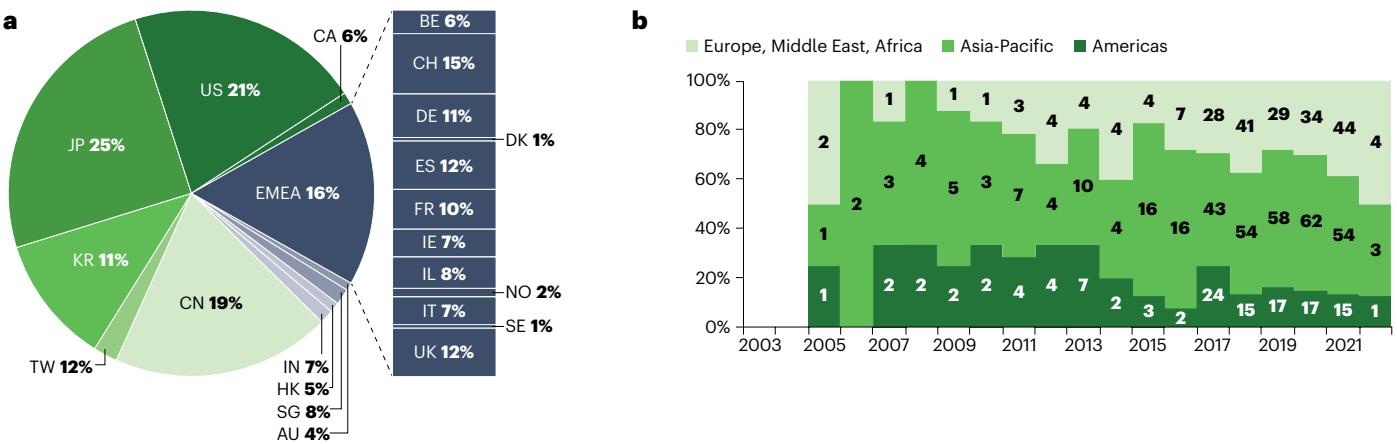

Fig. 1 | Where did East Asia get drug assets through licensing?. a, Overall distribution. US, United States; CA, Canada; BE, Belgium; CH, Switzerland; DE, Germany; DK, Denmark; ES, Spain; FR, France; IE, Ireland; IL, Israel; NO, Norway; IT, Italy; SE, Sweden; UK, United Kingdom; AU, Australia; SG, Singapore; HK, Hong Kong; IN, India; CN, mainland China; TW, Taiwan; KR, South Korea; JP, Japan. **b**, Breakdown by time.

decreased while those in mainland China have increased from 10.5% in 2015 to 46.7% in 2021 (for out-licensing) and from 18.2% in 2015 to 43.9% in 2021 (for in-licensing).

Knowledge diffusion

It is also helpful to break down the statistical scope of licensing projects into individual jurisdictions in East Asia. This shows a more detailed but different result compared with the previously established United States–Japan–South Korea–Taiwan–mainland China route.

For the out-licensing projects initiated in East Asian jurisdictions (and also the United States), focuses were on Japan first, but then shifted to South Korea and more recently to mainland China. Taiwan has never received a sizable number of out-licensing projects, and hence may not prove a pivotal link in this route. In brief, for stakeholders interested in the East Asian markets, the changes in out-licensing focuses can be described as a shift toward a United States–Japan–South Korea–mainland China route (Fig. 3a–d).

For projects in-licensed to East Asia, the major sources were the United States first, and then Japan or mainland China. Finally, a localization milestone may be reached: local drug patents have become the top-priority source for in-licensing. This localization milestone appeared first in Japan, then in South Korea and afterward in mainland China. This milestone has not yet arrived in Taiwan. South Korea and Taiwan do not output a large number of drug patents to neighboring jurisdictions in East Asia. Therefore, the top-priority in-licensing sources of East Asia usually conform to a shift toward a United States–Japan or China–domestic route (Fig. 3e–h).

The general trend can be interpreted through the gradient from deep to light color in Fig. 3. However, an opposite trend from light to deep color can be observed in South Korea and Japan from 2019. These countries tend to in-license more drugs from the United States and Japan and to out-license more drugs into Japan and South Korea, but not into Taiwan and mainland China. This countertrend may have been caused by the US–China trade war of 2018 and China's strict restrictions on international intercourse due to the COVID-19 outbreak in 2020.

A positive sign for mainland China is that it has not only become the top source of in-licensing projects to Taiwan, but also the only developing country that can continuously output its drug patents to the Japanese market. This reveals technological catch-up by mainland China, which is further analyzed in the following section.

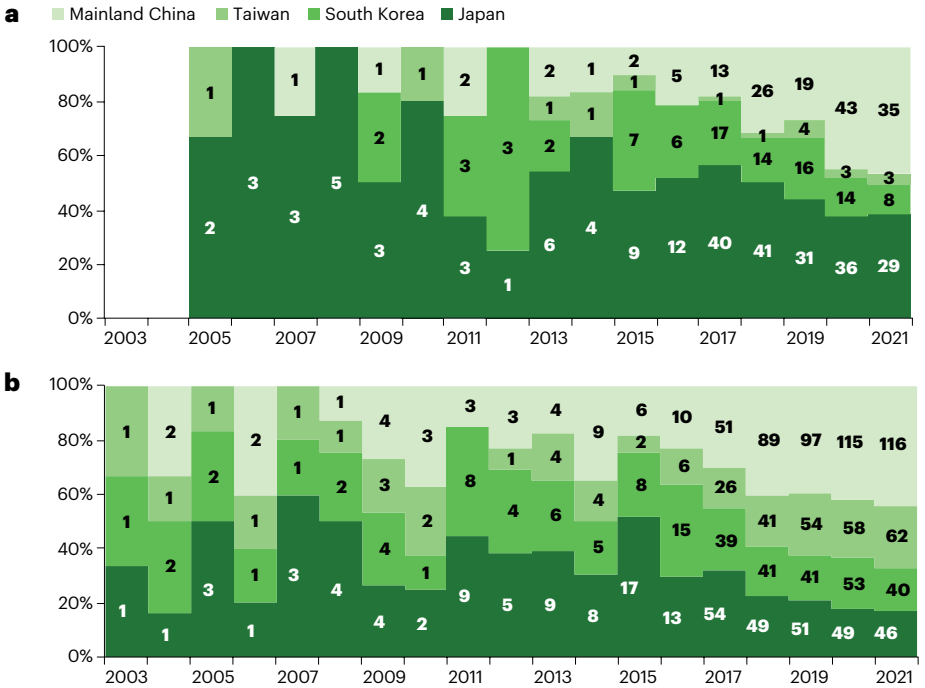

Fig. 2 | Spatial evolution of licensing projects in East Asia. a, Out-licensing projects from East Asia. **b**, In-licensing projects to East Asia.

Technological catch-up

Previous research has introduced a patent self-citation rate as an indicator to track the technological catch-up among East Asian regions in the memory chip industry[7]. Similarly, the concept of a 'self-licensing' rate can be used, with the term defined as a licensing activity in which the licensee and licensor are from the same jurisdiction; that is, the jurisdiction in which the licensing project is implemented.

The self-licensing rate indicates that 49.7% of in-licensed projects in Japan in the last two decades (2003–2022) were initiated by Japanese corporations and research institutions. After Japan's come self-licensing rates for South Korea (33.8%), mainland China (31.4%) and Taiwan (7.8%). These self-licensing rates of East Asian jurisdictions can also be broken down by time, although data are not available for every year (Fig. 4a). The self-licensing rate in mainland China has increased from 2017 and exceeded that of South Korea in 2020. Meanwhile, the self-licensing rate in Japan is still the highest in East Asia, but has been slowly decreasing since 2015.

A complementary indicator is the ratio of the number of out-licensed projects and in-licensed projects, which can also be used to evaluate biopharmaceutical advancement in East Asia. Here, Japan (96.7%) again ranks first, followed by South Korea (66.2%) and mainland China (62.8%). Taiwan (13.3%) is the only jurisdiction in our sample regions that has not reached a localization milestone. In other words, local drug assets in Taiwan have not yet become the top priority of its in-licensing projects. After breaking down these ratios by time, a line chart also suggests that mainland China (72.9%) outstripped South Korea (57.3%) in 2020 (Fig. 4b). On the whole, the aforementioned two indicators demonstrate together that mainland China has caught up with South Korea and leapfrogged Taiwan in terms of drug licensing.

Theoretical reflections and conclusions

As the biopharmaceutical sector operates with its own logic and features, the diffusion trends of drug licensing may not follow the clear and linear route of other sectors as previously assumed. According to the Sankey (Fig. 5) and chord diagrams (Fig. 6), the licensing route from the United States to Japan, to South Korea, to Taiwan and mainland China only accounted for a small fraction of the total licensing network in East Asia. Instead, the more likely routes are the

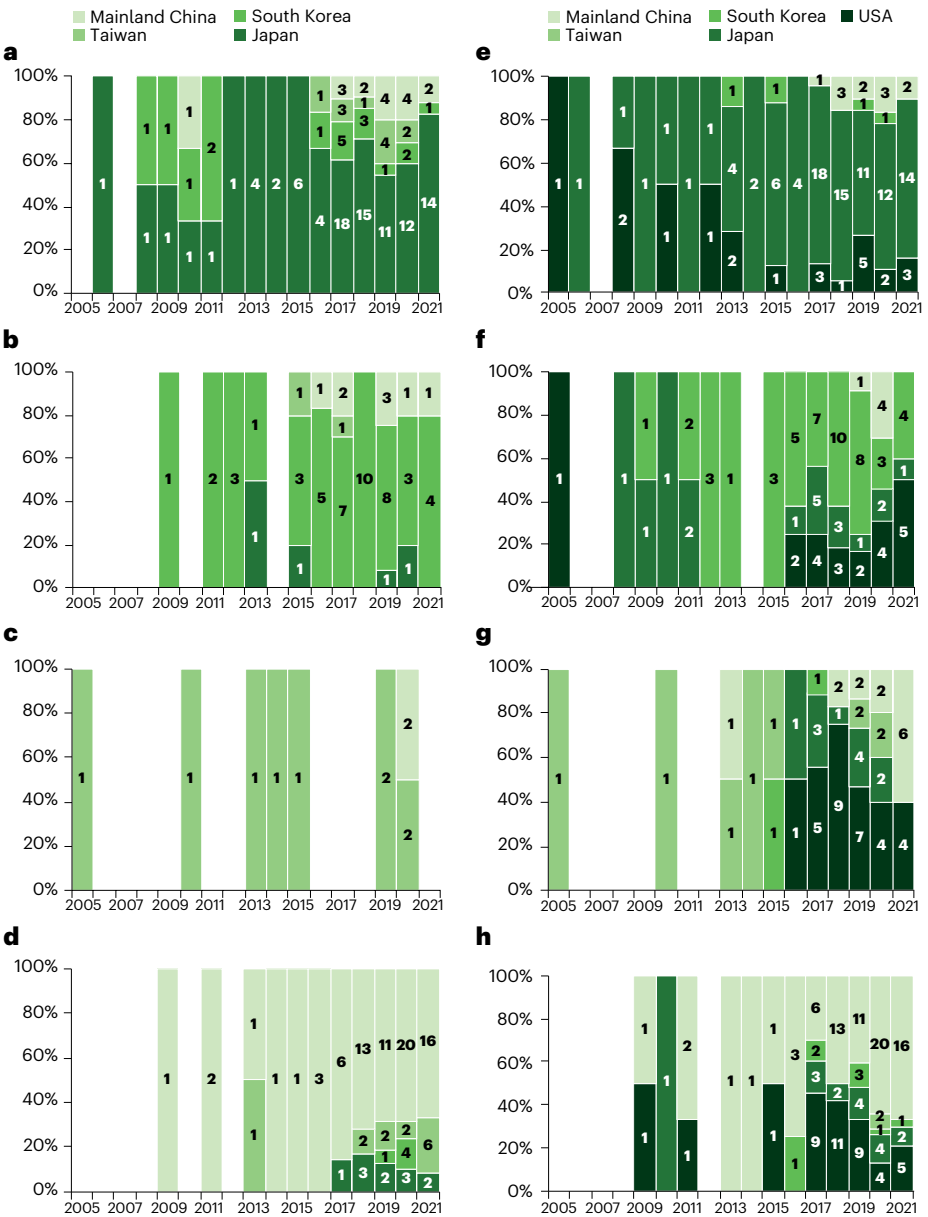

Fig. 3 | Knowledge diffusion of licensing projects in East Asia. Out-licensing projects from **a**, Japan, **b**, South Korea, **c**, Taiwan and **d**, mainland China, and in-licensing projects to **e**, Japan, **f**, South Korea, **g**, Taiwan and **h**, mainland China.

United States–Japan–South Korea–China for knowledge outputs and United States–Japan or China domestic for knowledge inputs. Furthermore, these routes are so weak that they may be stopped anywhere when domestic biotech R&D sectors grow or political or health crises occur. These findings not only deepen our real-world knowledge of drug patent licensing and external innovation dynamics, but also benefit the theoretical understanding of knowledge diffusion and technological catch-up in East Asia.

Reflective discussions and theoretical analyses can guide biopharmaceutical companies as to whether and where to locate their licensing focus. As mature and multinational companies are relatively inactive in developing East Asian markets through patent licensing and early-stage collaboration, this leaves the developing markets to small and medium-sized enterprises. As such, a data-driven perspective on licensing trends in East Asia reminds biopharma companies to approach licensing with a more reasonable resource configuration among different geographical locations, enabling them to adjust their licensing focuses and portfolio strategies in advance for R&D excellence. This would further help multinational corporations to avoid inefficient licensing[8–10] and to deal with challenges from latecomer firms. While there are already many well-developed lessons about the successes of latecomer firms[11,12], practical strategies for traditional giants to cope with latecomer firms remain underexplored but desired.

In-depth insights also highlight the valuable role of transnational licensing in accelerating biopharmaceutical knowledge diffusion and advancing health and well-being in developing regions. The lack of frontier technologies in developing regions has long been a global health dilemma[13]. Worse still, the social-responsibility and ethical aspects of drug licensing, such as the applications of licensing to rare diseases and regional diseases in the global South, are often overlooked[14,15]. This evidence-based analysis exhibits a beneficial transformation of licensing projects from newly developed regions (like Japan and South Korea) to developing regions (like Taiwan and mainland China). The paths and experience of the East Asian biopharmaceutical sector should be further encouraged and optimized to facilitate health advancement and improve policy implementation.

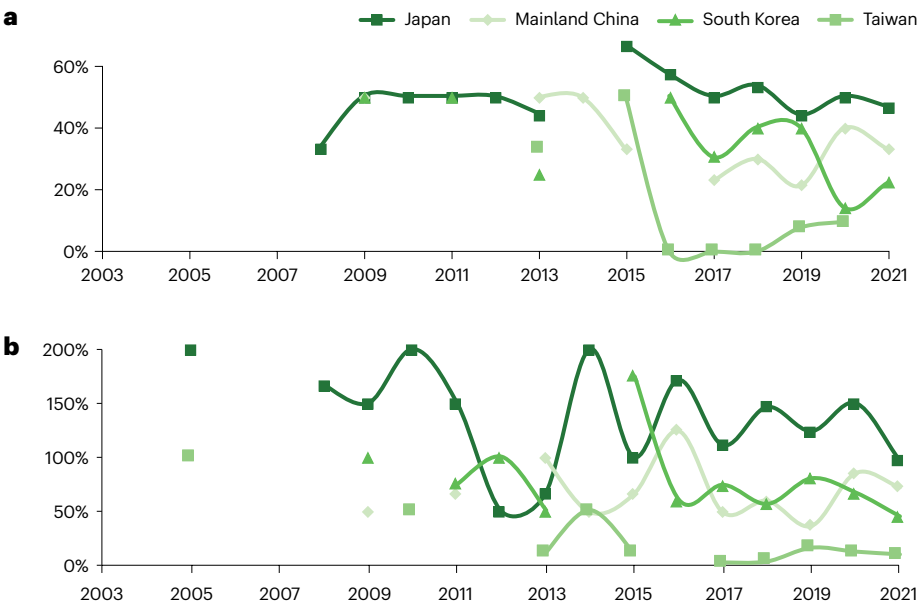

Fig. 4 | Pharmaceutical and biotechnology catch-up in East Asian countries. a, Self-licensing rate. **b**, Out-licensing/in-licensing ratio.

Fig. 5 | Licensing networks in East Asia. Out-licensing and in-licensing.

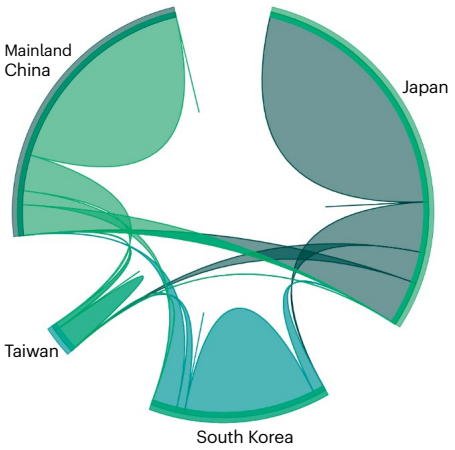

Fig. 6 | Licensing networks in East Asia. Self-licensing and transnational licensing.

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References

1. Lee, K. & Ki, J.-H. *Res. Policy* **46**, 365–375 (2017).
2. Wu, C.-Y. *Scientometrics* **98**, 429–446 (2014).
3. Hu, M.-C. *Res. Policy* **41**, 541–555 (2012).
4. Yan, W. *Nat. Med.* **21**, 968–971 (2015).
5. Huang, J. *Technol. Soc.* **67**, 101785 (2021).
6. Joly, Y. *Nat. Biotechnol.* **28**, 417–419 (2010).
7. Lee, K. & Yoon, M. *Technol. Anal. Strateg. Manage.* **22**, 553–570 (2010).
8. Kessel, M. & Hall, S. *Nat. Rev. Drug Discov.* **5**, 985–986 (2006).
9. Chitale, S., Lawler, C. & Macfarlane, S. *Nat. Biotechnol.* **31**, 362–363 (2013).
10. Featherstone, J. & Renfrey, S. *Nat. Rev. Drug Discov.* **3**, 107–108 (2004).
11. Liefner, I., Si, Y.-F. & Schäfer, K. *Technovation* **86**, 3–14 (2019).
12. Shin, J.-S. *Res. Policy* **46**, 404–416 (2017).
13. Keshi, C. B. *Value Health* **19**, A823 (2016).
14. Guebert, J. M. & Bubela, T. *Sci. Transl. Med.* **6**, 260cm11–260cm11 (2014).
15. Guerrini, C. J., Curnutte, M. A., Sherkow, J. S. & Scott, C. T. *Nat. Biotechnol.* **35**, 22–24 (2017).

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Competing interests

The author declares no competing interests.

Additional information

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