Australian National University

National Security College

A strategy for Quad biotechnology collaboration

Quad Tech Network

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About this paper

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NSC's publications comprise peer-reviewed research and analysis concerning national security issues at the forefront of academic and policy inquiry. This paper has been written as part of the Quad Tech Network initiative, and would not have been possible without the generous insights and advice provided to the authors in interviews with a number of experts.

About the Quad Tech Network

The Quad Tech Network (QTN) is an initiative of the NSC, delivered with support from the Australian Government. It aims to establish and deepen academic and official networks linking the Quad nations – Australia, India, Japan, and the United States – in relation to the most pressing technology issues affecting the future security and prosperity of the Indo-Pacific.

Contents

Key points

- Modern biotechnology includes the ability to easily edit the DNA of all living organisms like single cell organisms (such as yeast), viruses, plants and humans. It is the ability to edit life itself cheaply, quickly, and easily which will cause significant economic and social disruption.
- The global industrial system will be transformed as the world substitutes chemical and extractive manufacturing processes with biological alternatives in a wide array of key industries such as medicine, industrial chemicals, food, fuels, environmental cleanup, construction materials and clothing.
- The countries and firms which control the intellectual property (IP) and manufacturing for biotechnology products will have the opportunity to leverage it for strategic gain.
- Most of the global biomanufacturing capacity and IP to meet this transformation is yet to be created. The Quad, due to its powerful but limited membership, is a suitable body for governments to multilaterally develop biotechnological IP and biomanufacturing to ensure that is not controlled by others.
- The environmental and human security risk to accidental or intentional misuse of biotechnologies, particularly the gene editing of viruses, is potentially catastrophic. This needs transparent rules for control of new biotechnologies. The opacity of single party states cannot be trusted to deliver this.
- Current Quad biotechnology collaboration at the research, industrial and government level is limited and should be improved.

Key recommendations

- Quad governments should jointly contribute funding for the following initiatives:
  - *A biomanufacturing construction fund to shore up the future of biotechnology supply chains in Quad countries*. Each Quad country already has some government funds going to biomanufacturing. A portion of these could be pooled to avoid duplication and be more strategic in the allocation of those funds.
  - *A Quad genetic engineering research and commercialisation fund to develop the underlying IP for future biotechnological products*. There are already funds available in each country, but this IP will be so consequential – and the commercialisation challenging enough – that it is worthwhile for Quad countries to each contribute money to a Quad-specific fund.
- Quad governments should undertake the following actions to boost Quad biotechnology collaboration:
  - Establish a *biotechnology research collaboration office* to reduce barriers to Quad biotechnology research collaboration. Should it prove successful, the research office could, in time, expand to cover other critical technologies.
  - Appoint a *national bioeconomy coordinator* in each Quad country.
  - Establish a *Quad biotechnology hub* in India to fuel collaboration on research and development (R&D) through to manufacturing.
  - Establish an *office for the harmonisation of biomanufacturing processes and regulations.*
- The Quad should pursue early wins on specific projects, such as:
  - *Joint disease surveillance*, building on US-India collaboration.
  - *RNA-based biopesticides*, building on a collaboration between the University of Queensland and the Maharashtra Hybrid Seeds Company.
- *Biorefinement projects*, building on pilot project between US company Mercurius and Queensland University of Technology (QUT) that produces bio-based fuels.

What is biotechnology and why does it matter?[1]

Modern biotechnology focuses on the ability to easily edit the DNA of living organisms to produce biological outputs. For example, using genetically engineered yeast to produce milk. The applications are extremely broad from vaccines to industrial chemicals. Biotechnology is not new, but three recent advances have revolutionised it.

The ability to easily edit and insert DNA in living organisms

While reading and manufacturing DNA has become simple, the challenge of precisely cutting existing DNA and inserting new DNA into living organisms is more difficult. However, this is being overcome through modern CRISPR technologies.[2]

With CRISPR, it is easiest to edit the DNA of less complex organisms. Genetic alteration of bacteria and other single-celled organisms (like yeast) is commonplace in labs and biotechnology startups. The editing of virus DNA too has become very straightforward. Editing more complex organisms like plants and humans is relatively easy when done at the earliest stages of life (when the human or plant is still only a few cells big). Thus, altering the DNA of crops to increase yield, nutrient content, and drought resistance has become routine with CRISPR technology.

Editing the DNA of fully developed large multicellular organisms like adult humans remains more complex, but is now possible. Numerous – highly expensive – approved therapies now exist which alter human DNA. Scientists envisage human DNA will eventually be edited cheaply through an intravenous drip.[3]

New techniques to optimise the manufacture of biological products at scale

After an organism has been genetically edited to produce a certain output, such as yeast being edited to produce milk, it is then necessary to produce a large quantity of that organism to make the product commercially viable. This traditionally required much trial and error to find the right conditions (such as temperature, pH, oxygen and mixing rate).[4]

1 The authors would like to thank government, industry, academic, and think tank interlocutors in all four Quad countries. You were so generous with your time and input which strengthened the paper enormously. Any errors or faults in the paper are the responsibility of the authors.

2 CRISPR (pronounced “crisper”) stands for Clustered Regularly Interspaced Short Palindromic Repeats. It is a relatively new method of genome editing that relies on proteins discovered in bacteria which act as molecular scissors. Newer CRISPR technologies also provide ways to insert DNA into an organism’s genome.

3 Fyodor Urnov, “We can cure disease by editing a person’s DNA. Why aren’t we?”, *New York Times*, 9 December 2022, https://www.nytimes.com/2022/12/09/opinion/crispr-gene-editing-cures.html.

4 S.Y. Lee et al, “A comprehensive metabolic map for production of bio-based chemicals”, *Nat Catal 2* (2019) https://www.nature.com/articles/s41929-018-0212-4#Sec30.

It was a slow and expensive process. Scientists previously used naturally-existing proteins to catalyse their reactions. Now, new synthetic proteins can be designed entirely by artificial intelligence (AI).

These are quicker to source and often more effective at producing outputs of interest.[5] The COVID-19 vaccine designed by the University of Washington was the first medicine to contain a protein designed by humans. AI can now develop similar proteins in seconds.[6] So, it is quicker to scale up new biotech processes.

The application of AI to large biological datasets

The collection of large amounts of biological data is being used to train AI. This is leading to AI-developed processes which are much faster and more accurate than human-designed processes. An example is the use of AI in prognosis. Complex, multi-gene interactions alter an individual's predisposition to certain diseases, meaning an individual's genome contains information that can help determine their risk of developing these diseases. AI can spot patterns invisible to humans in this genetic data, allowing a patient an individualised risk profile to help future testing to be directed toward the diseases most likely in that individual. From protein structure, to drug screening, AI is revolutionising how biological data is used.

5 Yoo-Sung Ko et al, "Tools and strategies of systems metabolic engineering for the development of microbial cell factories for chemical production", *Chem. Soc. Rev.* 49 (2020) https://pubs.rsc.org/en/content/articlepdf/2020/cs/d0cs00155d.

6 Ewen Callaway, "Scientists are using AI to dream up revolutionary new proteins", *Nature*, 15 September 2022, https://www.nature.com/articles/d41586-022-02947-7.

The strategic importance of biotechnology

These new biotechnologies are strategically important for four reasons.

First, many of the world's most valuable industries will either partially or fully transition to manufacturing via biological methods.[7] The scale of the economic transformation will be enormous. Boston Consulting Group estimates that by 2030, biologically engineered systems could be used extensively in manufacturing industries that account for more than a third of global output – a shade under $30 trillion in terms of value.[8] A recent McKinsey study argues that eventually, up to 60 per cent of inputs into the global economy could be made using biological processes, disrupting almost every global industry.[9] The countries that lead in this technology will get a significant economic boost, as well as leverage through control of new global industry supply chains.

Second, biotechnology will become important to deliver society's basic goods in health, food security, energy, and environmental management. The countries and companies that control the essential IP and the biotechnology manufacturing base will have the potential to control the supply of basic social goods as well as wide array of broader industrial goods. This will trigger ethical conversations about how biotechnology should be used and distributed, due to its ability to meet human life's basic needs.

Third, there are clear security concerns surrounding modern biotechnologies. The ability to cheaply alter the DNA of all living organisms opens the possibility of bioweapons and bioterrorism on a scale not seen before. The potential for accidents is significant. Biological systems are self-replicating, meaning if a pathogen or unforeseen biological reaction is released into the broader world, the consequences could be devastating. We need to create systems of rules that are highly transparent in the case of an accident or even intentional misuse of biotechnologies. Single-party states such as China do not have a strong record on biological transparency.

Finally, biotechnology is about the control and usage of the genetic data of all living organisms including human genomic data. Individual human genetic data is potentially identifiable, even if it has been anonymised, leading to concerns surrounding personal privacy. Human genetic data collected outside of China by Chinese genomics companies has been stored on China's National GeneBank.[10]

The Quad cannot wait to act on this technology. The countries that lead the technologies will get a huge economic boost, have better control over the supply and IP of some of the most economically and socially consequential goods, and also get the biggest say on the ethics and the security of a technology that has the potential to be extremely devastating.

7 "The Bio Revolution: Innovations transforming economies, societies, and our lives," *McKinsey Global Institute*, 13 May 2020, https://www.mckinsey.com/industries/life-sciences/our-insights/the-bio-revolution-innovations-transforming-economies-societies-and-our-lives.

8 "Synthetic Biology Is About to Disrupt Your Industry", *Boston Consulting Group*, 10 February 2022, https://www.bcg.com/publications/2022/synthetic-biology-is-about-to-disrupt-your-industry

9 "The Bio Revolution", *McKinsey Global Institute*.

10 Kirsty Needham and Clare Baldwin, "China's gene giant harvests data from millions of women," Reuters, 7 July 2021, https://www.reuters.com/investigates/special-report/health-china-bgi-dna/

Building the fundamentals to lead on biotechnology

Challenge one: the biomanufacturing capacity shortage

Biomanufacturing is key to gaining the lead in modern biotechnology. All new products manufactured by genetically engineered organisms need to be produced somewhere. There is a huge deficit in the current global biomanufacturing capacity. The Good Food Institute predicts that 1000 times more capacity will be required just for alternative protein production by 2030, which far outstrips the projected capacity being created.[11] Alternative proteins is one small slice of biomanufacturing. This shortage is being replicated across every sector.

Innovation is beginning to suffer as companies place early-phase projects on the back burner due to a lack of biomanufacturing capacity.[12] In Australia, startups with promising technologies have had to wait years to get access to biomanufacturing capability.[13] This puts them at a disadvantage to competitors.

It is the scale-up to large biomanufacturing that remains the key bottleneck. According to the Boston Consulting Group, more than 90% of synthetic biology technologies fail because they can't be scaled.[14]

The key point still remains: genetic engineering is no longer the challenge, it is the move to scale. This failure rate puts off potential biomanufacturing investors who want clearer returns. The scale-up challenge will need government intervention.

There are thousands of companies currently engineering organisms that will eventually require vast biomanufacturing capacity. For example, Samsara Eco (an Australian company) is beginning to scale up production of company-engineered enzymes that break down plastic to its original form – there is a lot of plastic in the world, so they will need to produce a lot of enzymes.[15] EdenBrew (an Australian company) genetically engineers yeast to produce milk through fermentation.[16] Bioweg (a German company) has developed a novel strain of cellulose that substitutes for synthetic polymers like polystyrene which are used in plastics, cosmetics and oils.[17] BeiGene (a company headquartered in China and the US) has developed numerous humanized monoclonal antibodies to treat cancers,[18] a technology which has applications across numerous human diseases.

The countries that can provide scale-up opportunities will be in the best position to lead on biotechnology, and thus have strategic leverage over the supply chain. China is taking biomanufacturing very seriously.

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11 "2021 Fermentation State of the Industry Report", *Good Food Institute*, https://gfieurope.org/wp-content/uploads/2022/04/2021-Fermentation-State-of-the-Industry-Report.pdf.

12 "Biomanufacturing Capacity Crunch: It's The Supply Chain's Fault," *Bioprocess Online*, 7 October 2022, https://www.bioprocessonline.com/doc/biomanufacturing-capacity-crunch-it-s-the-supply-chain-s-fault-0001.

13 Interviews held with Australian biotechnology startups in 2023.

14 "Synthetic Biology Is About to Disrupt Your Industry", *Boston Consulting Group*.

15 "Samsara Eco technology," *Samsara*, https://www.samsaraeco.com/our-technology.

16 "Milk without cows – how synthetic biology and dairy farmers can both win", *AgriFutures Evoke*, 1 December 2022, https://evokeag.com/milk-without-cows-synthetic-biology-dairy-farmers-both-win/.

17 "Biobased Alternatives to Synthetic Polymers with Bioweg," *Ginko Bioworks*, https://www.ginkgobioworks.com/2023/02/06/biobased-alternatives-to-synthetic-polymers-with-bioweg/.

18 "Development Pipeline," *BeiGene*, https://www.beigene.com/our-science-and-medicines/pipeline/.

Challenge two: competition from China

At this stage, Europe is the leader in biomanufacturing capacity globally.[19] But given the rapid changes in the industry, most of the future biomanufacturing capacity is yet to be built.

China is diverting huge amounts of resources toward capturing the biomanufacturing market as it did with small molecule active pharmaceutical inputs (APIs). Adrian van den Hoven, Director General of Medicines for Europe, states, "China and India are getting close to reaching the standards required for exporting biopharmaceuticals – and when this happens there is likely to be a lot of consolidation in the biopharma market."[20]

The same will eventually be true in other biomanufacturing sectors, even in a potentially less globalised world.

In a 2022 paper dedicated to the bioeconomy from China's National Development and Reform Commission, biomanufacturing at scale was a central theme across multiple applications such as plastics, oils, and industrial food production. The report states that there is a need to "solve the funding needs of companies for R&D and manufacturing."[21]

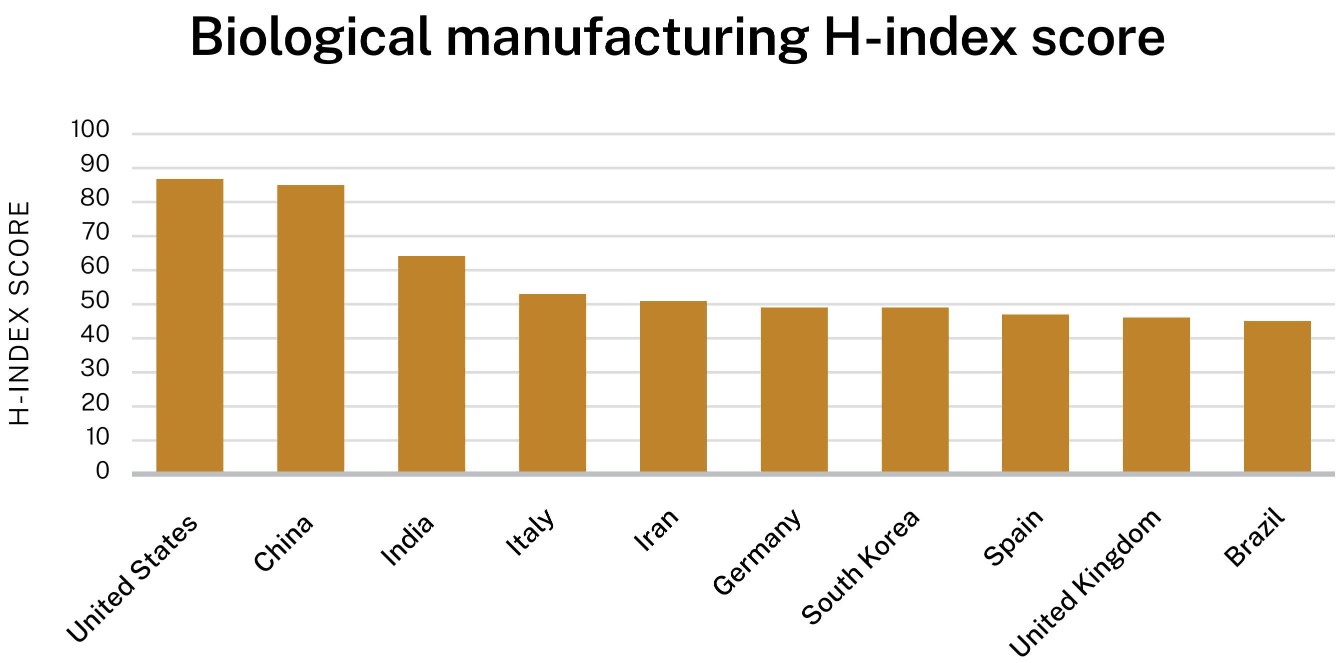

Figure 1 - Top 10 countries in biological manufacturing research output. Ranked by each country's proportion of publications in the top 10% of the most highly cited papers. Source: "Critical Technology Tracker", Australian Strategic Policy Institute, https://techtracker.aspi.org.au/tech/biological-manufacturing/?colours=true.

19 "State of Global Fermentation Capacity", *Synonym Biotechnologies Inc*, https://www.capacitor.bio/trends.

20 "Biopharma 2021 – The Resilience Rethink", *Cytiva*, https://cytivadelivery.sitecorecontenthub.cloud/api/public/content/digi-49915-original

21 "'14th Five-Year Plan' bio-economy development plan", *National Development and Reform Commission*, https://www.ndrc.gov.cn/xxgk/zcfb/ghwb/202205/P020220510324220702505.pdf.

Many countries have expressed similar sentiments, but China has successfully dominated manufacturing of emerging technologies in the past. The Australian Strategic Policy Institute Critical Technology Tracker shows that academics in China publish more of the top 10% most-cited academic papers for biomanufacturing than those in any other country.

By H-index (metric for evaluating the cumulative impact of an author's scholarly output) authors in China and the US are about equal.[22] Not all research leads to commercial products, but this is one important indicator to suggest that China is gaining rapidly on biomanufacturing. China's track record provides good reason to believe it will build its biomanufacturing base faster than its competitors.

Proportion of the top biological manufacturing publications

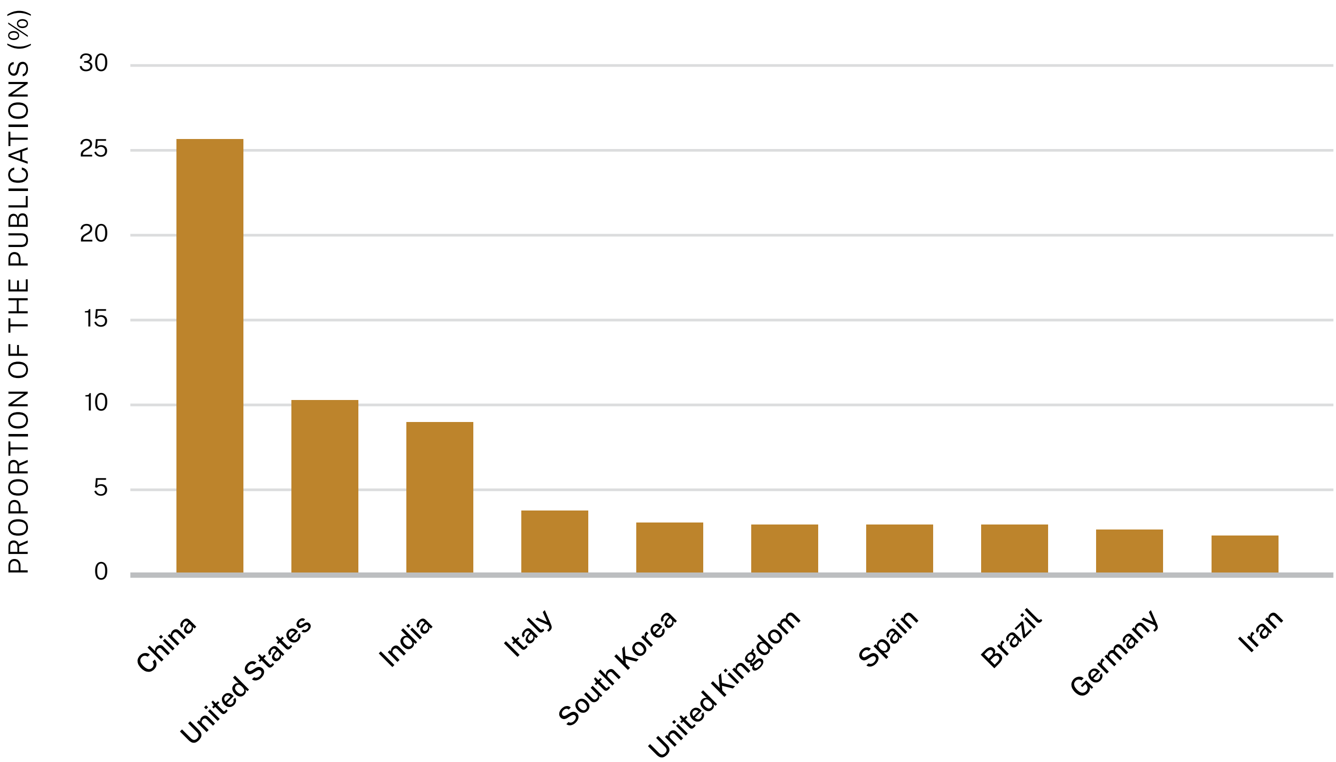

Figure 2 - Top 10 countries in biological manufacturing research output. Countries ranked by H-index. ASPI Critical Technology Tracker - https://techtracker.aspi.org.au/tech/biological-manufacturing/?colours=true.

22 "Critical Technology Tracker", *Australian Strategic Policy Institute*, https://techtracker.aspi.org.au/tech biological-manufacturing/?colours=true.

The solution: a joint Quad fund for bioreactor and fermentation construction

This paper suggests that Quad governments develop a joint fund for bioreactor and molecular farming construction to quickly shore up the future of biotechnology supply chains.

This fund should focus on two main categories of biomanufacturing facilities. The first category is bioreactors, in particular the demonstration-scale and large-scale facilities. Demonstration-scale facilities are typically larger than 500 litres (highly dependent on the type of output and organism used), which provide the capacity to demonstrate the commercial viability of a biomanufacturing process and product. These are much bigger than a typical lab facility which are often tens of litres. Large scale facilities are over 500,000 litres of capacity,[23] and provide enough means for economically viable production of biomanufactured goods. Access to the demonstration-scale and large-scale facilities is lacking globally, which particularly impacts companies that require economies of scale with a lower per-kilogram price for their product.[24]

The second category is plant-based molecular farms (PBMFs). These currently require more R&D but will be crucial for two reasons. The first is that, as the authors have come to learn from interviews with subject matter experts, there are space, biomass and material restrictions to building bioreactors at the scale that will be necessary to meet all biomanufacturing needs. The second is that PBMFs have the ability to reduce scale-up costs and increase scale-up speeds by enormous amounts. Therefore, targeting PBMFs and bioreactors will be crucial for the Quad to secure its position in the global biomanufacturing supply chain.

The funding could come in the form of loan guarantees, early-stage grants, and tax breaks. This should be ambitious, eventually in the order of billions of dollars. The US is likely to allocate significant extra government funding for domestic biomanufacturing. A small slice of that could be allocated to the Quad biomanufacturing fund.

In March 2023, the White House Office of Science and Technology Policy (OSTP) released its "bold goals for US biotechnology and biomanufacturing" paper.[25] It contains numerous ambitious goals for biomanufacturing to replace industrial chemicals, transportation fuels and small molecule (i.e., chemical) active pharmaceutical ingredients. The OTSP paper (and the associated White House fact sheet) did not allocate direct funding, but significant government money needs to be allocated to achieve the stated goals. When funding plans are developed for these goals, funds should be allocated to bringing other Quad members into this future supply chain.

The OTSP paper often focuses on the role of biomanufacturing in reducing US reliance on imports of critical goods. That is an understandable goal, but this goal will need to be achieved with partners. The risk is that US domestic biomanufacturing programs compete directly with programs from other Quad partners.

In the immediate term, the US Department of Defence (DoD) has recently announced $1.2 billion in funding to catalyse the growth of the US domestic biomanufacturing base.[26] The DoD also released a biomanufacturing strategy, stating "DoD will invest in biomanufacturing consistent with this Strategy to catalyse domestic biomanufacturing, protect biomanufacturing at home and with our allies and partners, and secure biotechnology and biosafety".[27] In line with this statement, a portion of the money from the DoD funds could be redirected to the Quad biomanufacturing

23 "State of Global Fermentation Capacity", *Synonym Biotechnologies Inc.*

24 See video at 23:13: "Commercial fermentation: Opportunities and bottlenecks," *Good Food Institute*, 14 May 2021, https://www.youtube.com/watch?v=aqr18eiot9Q.

25 "Bold goals for US biotechnology and biomanufacturing", *The White House Office of Science and Technology Policy,* March 2023, https://www.whitehouse.gov/wp-content/uploads/2023/03/Bold-Goals-for-U.S.-Biotechnology-and-Biomanufacturing-Harnessing-Research-and-Development-To-Further-Societal-Goals-FINAL.pdf.

26 "FACT SHEET: Biden-Harris Administration Announces New Bold Goals and Priorities to Advance American Biotechnology and Biomanufacturing," *The White House*, 22 March 2023, https://www.whitehouse.gov/ostp/news-updates/2023/03/22/fact-sheet-biden-harris-administration-announces-new-bold-goals-and-priorities-to-advance-american-biotechnology-and-biomanufacturing/.

27 "DoD Biomanufacturing Strategy", *United States Department of Defense*, 22 March 2023, https://www.cto.mil/dod-bioman-strat/.

fund as a starting point for US involvement in Quad biomanufacturing to be followed up with further funding as the OTSP plan matures.

Other governments in the Quad must be prepared to also contribute alongside the US. All Quad governments have money already being directed toward biomanufacturing in some capacity. At the subnational level in Australia, the New South Wales government funds "High-Throughput Fermentation, Analytical Screening and Startup Incubation at the Australian Genome Foundry" as part of the Emerging Industry Infrastructure Fund (EIIF).[28] Australia's National Reconstruction Fund, a fund dedicated to transforming Australia's infrastructure, supply chains and driving economic growth, sits as an ideal source of funds for Quad biomanufacturing.

To be clear, the current funds are not enough. There is a race on to develop biomanufacturing capability, and the winners will control large parts of the global supply and reap huge economic benefits.

While all four countries can establish their own biomanufacturing capacity, it is also vital that cross-border collaboration occurs to allow each Quad country to play to its strengths. India has a unique ability to compete in key biomanufacturing areas at scale in a way other Quad countries do not. Kiran Mazumdar-Shaw, the chairperson and founder of Biocon, India's largest listed biopharmaceutical firm by revenue, believes that India's approach to developing biopharmaceuticals provides a template for supply chain resilience that other countries can follow. "I think companies need to be global in their business models," she says. "Today, India is able to cater to large populations in low and middle-income countries because of our high-volume, low-value approach, which is really inbuilt in everything we do."[29]

Japan's long history with fermentation places it at the forefront of quality biomanufacturing processes, but it lacks large-scale capacity. Australia and the US have the advantage of producing significant amounts of inedible biomass, which is used as an input for biomanufacturing. The proximity of manufacturing biomass to R&D hubs can be useful in the scaling-up of production from research settings to commercially viable products, facilitating early prototyping that has been crucial for commercial success.[30]

Our proposed Quad bioreactor fund can speed this up. As one Australian investor told the authors, "If it takes five years, it will be too late." It must be tailored to country-specific needs with a clear set of priorities. There will inevitably be some waste, but the potential return is worth the risk. This will simultaneously help to manage both the capacity shortage challenges and the challenge of who leads in this technology.

28 "Synthetic Biology and Biomanufacturing", NSW Government and Chief Scientist, https://www.chiefscientist.nsw.gov.au/rdnsw/emerging-industry-infrastructure-fund/synthetic-biology-and-biomanufacturing.

29 "Biopharma 2021", 7.

30 "Accelerating the Biomanufacturing Revolution", *World Economic Forum*, February 2022, https://www3.weforum.org/docs/WEF_Accelerating_the_Biomanufacturing_Revolution_2022.pdf.

Building the fundamentals to lead on product and research IP

Challenge: Quad countries are not maximising their collaboration on biotechnology

The Quad countries are in a unique position to combine their complementary abilities in biotechnology R&D. Australia and Japan both have well-established R&D sectors and conduct world-class clinical trials and product testing. Yet both countries underperform in biotechnology research relative to their wealth and size, according to data from Cytiva.[31] The US leads the world in biotechnology R&D, but India is relatively nascent in its R&D capability, creating a space ripe for collaboration.

Despite these complementary capabilities, there are two research trends that should be of concern. First, research collaboration between non-US Quad members is relatively low.

Data taken from the SciVal database – exemplified by figures 3-6 below which compile the international co-authored publications in three key fields of biotechnology: biochemistry, molecular biology and genetics – demonstrate that all member countries naturally publish a large amount of collaborative research with the US. However, Australia, Japan and India undertake more research with China than they do with one another.

Second, China is steadily increasing its share of joint publications at the expense of the US. Collaboration with China represents a larger portion of Australia's total international publications over time, with the USA losing its some of its share. This trend is mirrored in both India and Japan, where the smaller Quad members represent a very small portion of each other's collaborative research.

31 "Biopharma 2021", 20.

Australia's international biochemistry, genetics and molecular biology research collaboration

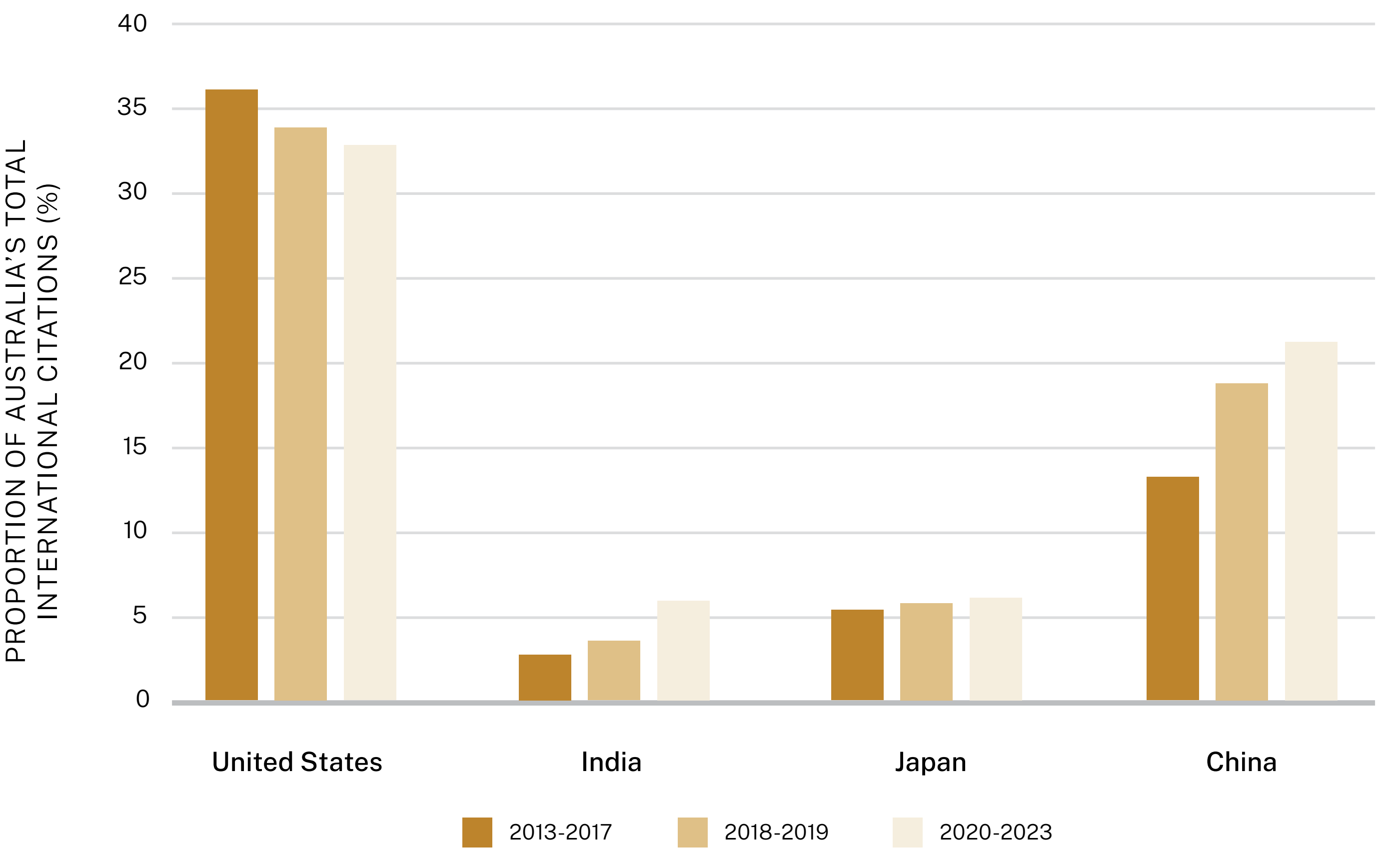

Figure 3: Australia's international partners in biochemistry, genetics and molecular biology research as a proxy for biotechnology. Proportion of co-authored publications in these fields with each of the Quad partners and China. Data gathered using SciVal database from Scopus, containing data from 2013 to June 2023.

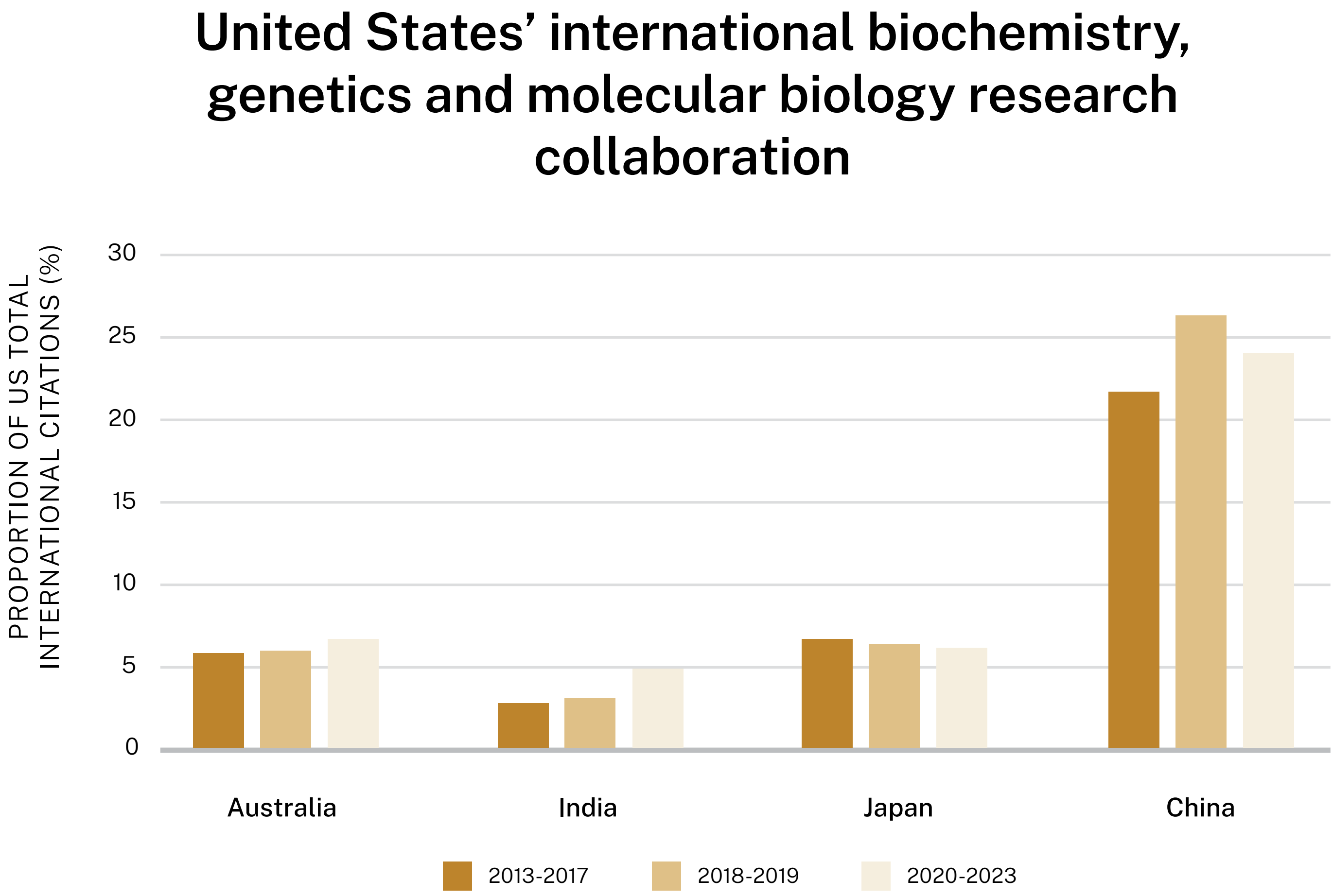

Figure 4: US international partners in biochemistry, genetics and molecular biology research as a proxy for biotechnology. Proportion of co-authored publications in these fields with each of the Quad partners and China. Data gathered as in Figure 3.

Japan's international biochemistry, genetics and molecular biology research collaboration

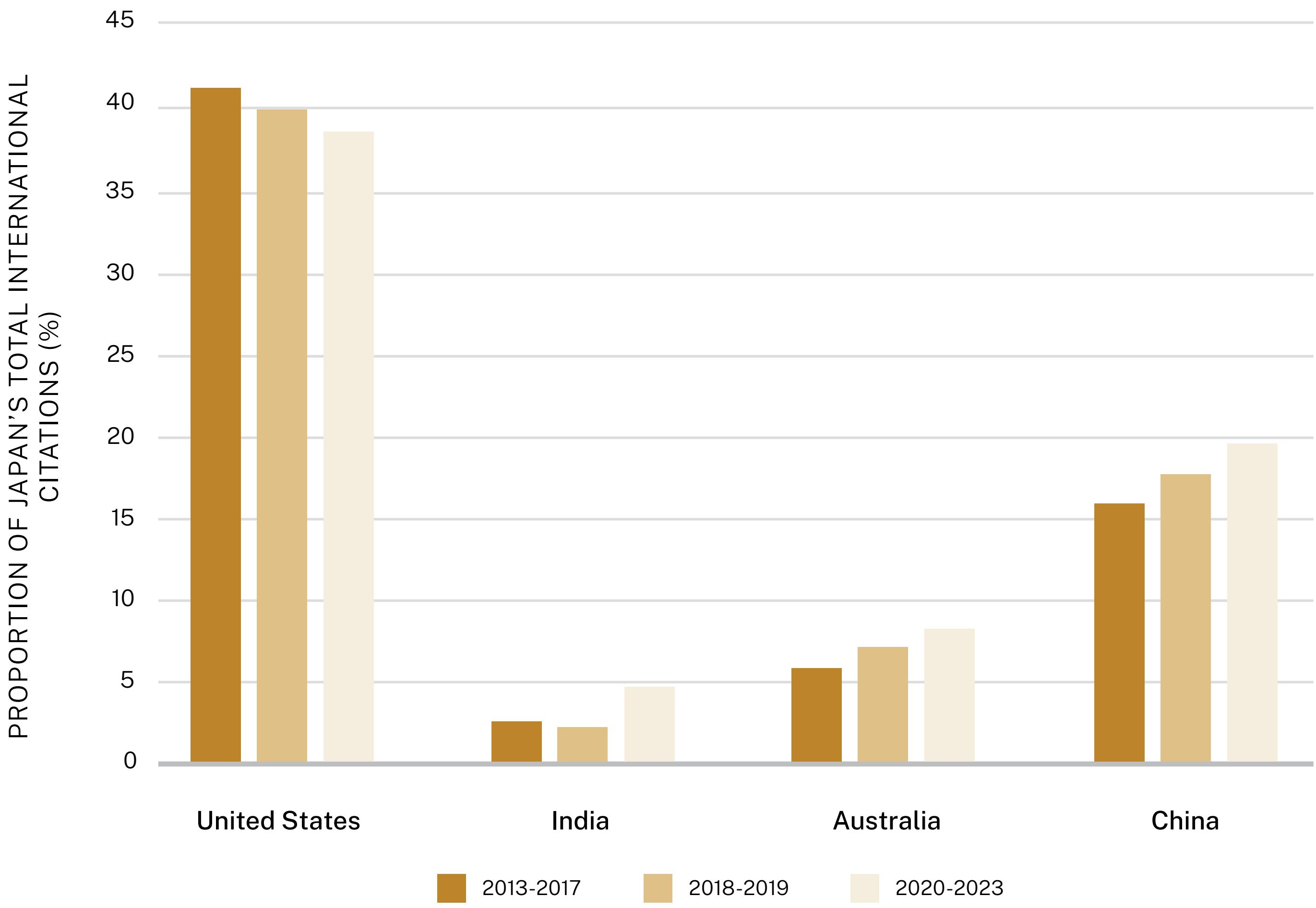

Figure 5: Japan's international partners in biochemistry, genetics and molecular biology research as a proxy for biotechnology. Proportion of co-authored publications in these fields with each of the Quad partners and China. Data gathered as in Figure 3.

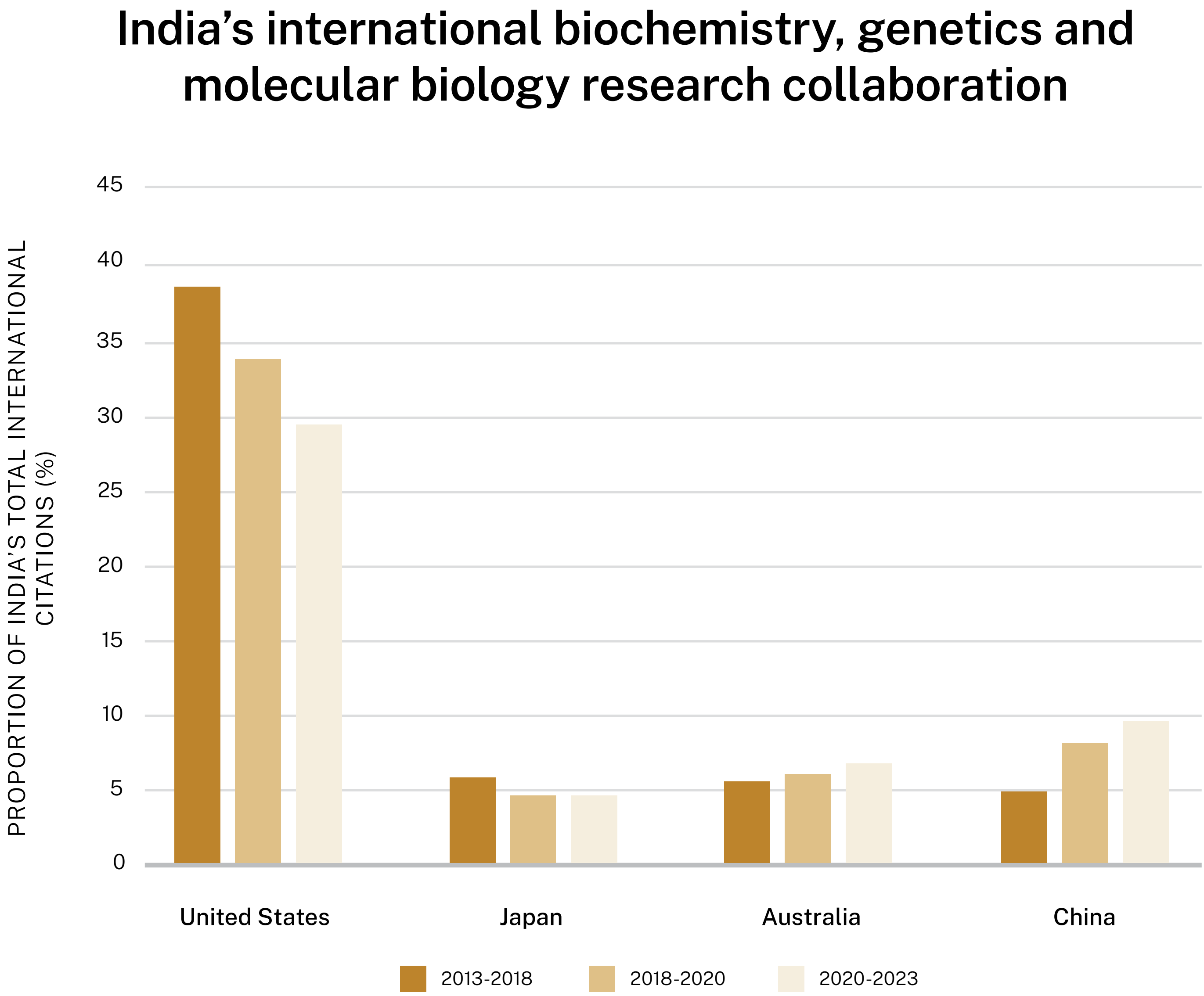

Figure 6: India’s international partners in biochemistry, genetics and molecular biology research as a proxy for biotechnology. Proportion of co-authored publications in these fields with each of the Quad partners and China. Data gathered as in Figure 3.

Solution one: lowering barriers to research collaboration

This paper recommends numerous policies to lower the barriers of research collaboration. Firstly, the establishment of a Quad biotechnology research collaboration office. This office would:

i. *Coordinate an infrastructure and capability delivery fund*. Many key pieces of infrastructure are required to acquire or build to develop a thriving R&D environment, but many researchers across the Quad are unable to quickly and efficiently access them.

ii. *Facilitate training across member countries on cutting-edge biotechnology techniques and equipment*, such as flow cytometry, bacterial and viral transformation, and high throughput genetic screening.

iii. *Streamline visas for biotechnology researchers applying to conferences or cross-border training in other Quad countries*. Researchers told the authors that invitation letters for conferences are sent out 8-10 weeks in advance. It currently takes 10 weeks to get a visa interview with US missions in India.

iv. *Reduce travel and visa costs across Quad countries*. This would include a stipend for international biotechnology researchers going to other Quad countries for work. This is a barrier to researcher collaboration and network building across all countries.

v. At a later stage, the office could be *extended to other countries in the Indo-Pacific*.

The proposed travel subsidies remove the cost barriers to attendance at important conferences for junior researchers, particularly from India.[32] This would build upon the Quad's pre-existing fellowship program by allowing a much broader base of researchers from each country to interact with each other.

There are multiple bilateral scientific exchange programs already between Quad countries. For example, the Japan Society for Promotion of Science (JSPS) have partnered with the Australian Academy of Science to provide postdoctoral exchange between the two nations in key scientific fields.[33] Another example is the Australian Research Cooperation Hub India (ARCH-India). This hub aims to increase the amount of collaboration between the two nations through identifying major sources of funding, increasing the awareness of the complementary strengths, and increasing researcher mobility.[34] The Quad biotechnology research collaboration office should attempt to make these programs quadrilateral, or at least act as a catalyst for trilateral action between Quad states if full consensus can't be reached by all four nations. It also helps to reduce the duplication of bilateral programs.

32 Interviews with biotechnology researchers conducted by the authors between November 2022 and February 2023.

33 "Japan Society for the Promotion of Science fellowships", *Australian Academy of Science*, https://www.science.org.au/supporting-science/awards-and-opportunities/japan-society-promotion-science-fellowships.

34 "About", *ARCH-India*, https://arch-india.org/about.

Program Title	Countries Involved	Synopsis
Australia-India Strategic Research Fund (AISRF)	Australia and India	Funds research across 20 different mutual STEM interests, including biotechnology, stem cells and biomedical devices.
Australia-Japan Foundation grants	Australia and Japan	Wide-ranging grant that is partly directed towards scientific innovation.
ARCH-India	Australia and India	Set up in 2021 to encourage and streamline research collaboration between the two countries.
National Science Foundation (NSF) and National Institutes of Health (NIH) funding	US and external countries	The US has fewer dedicated bilateral funds, instead allowing research collaboration through internal funds more easily.
India-Japan Cooperative Science Program (IJCSP)	India and Japan	Supports bilateral scientific collaboration, particularly focusing on fundamental sciences, materials and system engineering, life sciences, biotechnology and mathematics.

Current major collaborative research efforts between Quad countries.

Another barrier is the speed of visa approval for short-term visits to the US for Indian researchers. It takes on average 63 days to get an interview for a visa application at US missions in India, and even longer to obtain the visa.[35] One option is to simply speed that up, which the US government is in the process of doing.[36] A more innovative approach is to offer a suite of rapidly-approved visas through the research collaboration office that are flexible, quick, and can allow many opportunities, such as six-month lab secondments at short notice.

Finally, and most importantly, the proposed research collaboration office would provide biotechnology infrastructure funds and training. The industry is changing so rapidly that constant upgrades to lab infrastructure and concurrent training are vital to competitiveness, particularly outside the US. One clear message from interviews with Indian researchers is that research training would ideally happen in India, perhaps through a permanent facility. There are concerns around brain drain, and it is important that the Quad is seen to be contributing to building out India's capabilities.

35 The State Department website indicates that visa interview waiting times at the US Embassy in New Delhi for Students/Exchange Visitors (F, M, J) are 63 days (as of 16 May 2023) https://travel.state.gov/content/travel/en/us-visas/visa-information-resources/wait-times.html.

36 Rezaul H Laskar, "US launches more initiatives to cut wait time for visa applicants", *Hindustan Times*, 22 Feb 2023, https://www.hindustantimes.com/india-news/us-launches-more-initiatives-to-cut-wait-time-for-visa-applicants-101674397714234.html.

Solution two: the creation of a Quad genetic engineering research and commercialisation fund to target capital towards the most consequential research

This will include funding research into new targeted CRISPR therapies, AI generation of novel metabolic pathways and proteins, as well as high-throughput genetic screening to accelerate the development of novel, safe biotechnology outputs.

Alongside biomanufacturing, occupying the heights of genetic engineering will play a disproportionate role in ensuring control over supply chain IP. It is genetically engineered organisms that will drive new valuable biological products. Thus, ensuring Quad countries are at the cutting edge in each is imperative.

This fund would serve as top-up or extension funds for projects involving collaborators from Quad countries. In interviews with researchers in Japan and India, the authors were told that current programs do not cover a long enough time period to get genetic engineering research to the pre-commercial stage. This fund would be focused on the underlying genetic engineering IP which is separate from the manufacturing. Thus, we have proposed these as separate funds with distinctly different purposes, but they could still be administered from the same office.

US expertise in the commercialisation of such output is the most developed of Quad partners, as shown by 15 of the top 30 largest biotechnology companies globally being US companies.[37] Commercialisation training could be offered in addition to the funding to ensure that Quad partners have the best chance of commercialising their breakthroughs.

Solution three: the establishment of a Quad biotechnology hub in India to fuel collaboration on R&D in biomanufacturing

India has the benefit of a large, established infrastructure and expertise in pharmaceutical manufacturing, as well as many biotechnology start-ups. It is seeking to boost its R&D capability but as noted above, is confronted with significant concerns around brain drain.

India already has biotechnology hubs, which should be leveraged by the Quad. This should involve setting up permanent training facilities in reputed research universities in or around the hub and attracting local biomanufacturing startups to grow India's R&D output.[38] The recent policy changes in India, which allow the establishment of foreign universities, can encourage scholar exchange programs. The Indian office for Quad research collaboration (one of the proposals in this paper) could be situated in the hub, as could the offices for the various funds suggested in this paper. This hub would serve as a nexus for capital, training, equipment and regulation efforts occurring in the biotechnology space.

37 "Biotechnology Industry Overview: Latest Market Statistics", *Getthrough*, https://www.gethrough.com/biotech-industry-overview/.

38 This idea grew from a discussion with Shambhavi Naik, Saurabh Todi, and others at the Takshashila Institution in Bengaluru. The authors are thankful for their input and ideas.

Building a shared understanding of biotechnology vision, language, values and regulations

The broad applications of new biotechnologies mean that coordination within and between countries is difficult. This paper recommends the **appointment of a national bioeconomy coordinator within the government of each of the Quad countries.** These figures will meet regularly alongside the Quad's Critical and Emerging Technologies Working Group to guide structured discussion on each country's biotechnology landscape. They also offer an important point of contact. The technology is so diffuse that decision-making sits inside many different departments (health, agriculture, industry, standards etc).

In our view, these roles would be more centralised than the State Department's new Tech Envoy's office Biotechnology Policy Coordinator.[39] It would also vary from the State role in that it is Quad-specific. Similar appointments could be made for other technologies if deemed necessary.

The national bioeconomy coordinators could also oversee **an office for the harmonisation of biomanufacturing standards, processes and regulations.** This office would:

- *Establish common language* around biotechnology and biomanufacturing standards.
- *Develop common ground on manufacturing regulations.* It may not be possible to have complete harmonisation, but it should be possible to identify areas in which regulations can be harmonised.
- *Develop an ethical and social licence unit* to begin finding common ground between the four countries.

These tasks will have a much longer timeline than providing capital through funds, but they are important.

39 "About Us: Office of the Special Envoy for Critical and Emerging Technology", United States Department of State, https://www.state.gov/about-us-office-of-the-special-envoy-for-critical-and-emerging-technology/.
The current Biotechnology Policy Coordinator in the office is Megan Frisk.

At an ethical and social licence level, this is the first building block in generating commonality between some of the biggest democracies in the Indo-Pacific. The future of biotechnology is up for grabs. The Quad is an attractive grouping for this process because it only requires four negotiating parties, but they are of a consequential size. If we do not set up systems which are transparent, equitable and safe, then the damage to humanity will be enormous. China's secrecy during COVID and previous pandemics has repeatedly demonstrated that it will not be open and transparent when there are biological accidents or disasters.

At a business level, it will allow for a simpler transfer of manufacturing capacity if the IP is produced in one country, but early manufacturing trials occur in another Quad country. The storage, packaging and transportation of bioproducts are more technically challenging than traditional chemical outputs, increasing the importance of a clear regulatory environment that reaches down to local bioreactor capacity. The downstream processes could be integrated into this harmonisation process too. By having a clear understanding of the biomanufacturing standards, processes and regulations in each Quad country, the barrier to entry into these markets is lower. Further flow-on effects of attracting significant private investment will also occur due to the more predictable regulatory environment.

Early project wins

The preceding recommendations in this paper are designed to set the Quad up for long-term success in biotechnology. It is also vital to facilitate early project-level wins to generate momentum. One potential approach is to build upon successful projects already underway via initiatives such as AISRF and USAID India projects. Initial scanning suggests there are several potential projects ripe for expansion:

- *An RNA-based biopesticides project between the University of Queensland and the Maharashtra Hybrid Seeds Company to create biopesticides*. This project leverages RNA interference technology to create a biopesticide that can kill fungal pathogens through a new mechanism of action, thus working on resistant pests. The Australian Research Council's research hub for sustainable crop protection at the University of Queensland has partnered with a huge range of Australian and international institutes. Bolstering food security is a major priority of all Quad countries, as well as the Asia-Pacific region. Therefore, this project can potentially be expanded to these regions, with existing finances being topped up by one of the proposed funds in this paper.
- *A biorefinement pilot project between US company Mercurius and Queensland University of Technology (QUT) that produces bio-based fuels*. The plant built in Mackay utilises bagasse, a waste product from sugarcane process supplied by nearby sugarcane mills, to create jet fuel and diesel. This plant is currently at a demonstration scale and shows commercialisation potential. Additional Quad funds could expedite this process and also lay the foundation for international partnerships in bio-based products.
- *Disease surveillance projects*. India, the CDC, and USAID already collaborate on disease surveillance. Australia has significant experience working on disease surveillance abroad through the Indo-Pacific Centre for Health Security. These pre-existing projects could be rolled into a harmonised Quad effort, probably first within India but then potentially in other Indo-pacific countries.

Conclusion

Biotechnology is a crucial emerging technology that promises to impact every facet of human existence over the coming decades. The Quad faces multiple roadblocks in securing the economic, strategic and environmental benefits biotechnology offers, including a biomanufacturing capacity shortage, competition from China and a lack of collaboration on fundamental and translational research. To overcome these barriers, the Quad must undertake multiple tasks simultaneously.

To address the biomanufacturing capacity crisis, we recommend the Quad fund key infrastructure in the supply chain, helping to create reliable and efficient supply networks across a multiplicity of products. In order to compete with China in this space, we urge the Quad to formalise their cooperation, working together to create the IP that will change the world. This should be facilitated by focusing on key technologies, such as genetic engineering, as well as better facilitating the commercialisation of research. To this end, we recommend a genetic engineering and commercialisation fund, as well as a research collaboration office to efficiently direct capital and effort. Finally, the Quad must be seen to create fast headway, targeting early wins that demonstrate the worthwhile contribution the Quad can make to biotechnology. The recommended projects above should provide a starting point for this process. To facilitate this process long term, we also recommend that the Quad should make efforts at developing commonalities surrounding regulations, language and ethics in biotechnology. While not all of this will be easy, the Quad is an ideal size to undertake such a task. If done correctly, this could lay the foundation for the future of biotechnology for its members, the Indo-Pacific, and beyond.

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