

## South-South entrepreneurial collaboration in health biotech

Halla Thorsteinsdóttir, Christina C Melon, Monali Ray, Sharon Chakkalackal, Michelle Li, Jan E Cooper, Jennifer Chadder, Tirso W Saenz, Maria Carlota de Souza Paula, Wen Ke, Lexuan Li, Magdy A Madkour, Sahar Aly, Nefertiti El-Nikhely, Sachin Chaturvedi, Victor Konde, Abdallah S Daar & Peter A Singer

**A survey of entrepreneurial collaborations among health biotech firms in developing countries reveals a surprisingly high level of collaboration but a lack of emphasis on new or improved health biotech products and processes.**

In recent decades, developing countries have sought to reduce their reliance on trade with the economically and politically dominant northern, or developed, countries, favoring instead South-South partnerships that synergize strengths and bolster competitiveness. Entrepreneurial firms in developing countries are increasingly aware of the opportunities in one another's markets, as is evident from the 12.5% increase in the rate of South-South trade each year<sup>1</sup>.

Emerging economies, such as China and India, have experienced unprecedented growth

*Halla Thorsteinsdóttir, Christina C. Melon, Monali Ray, Sharon Chakkalackal, Michelle Li, Jan E. Cooper, Jennifer Chadder, Abdallah S. Daar and Peter A. Singer are at the McLaughlin Rotman Centre for Global Health, University of Toronto and University Health Network, Toronto, Ontario, Canada. Halla Thorsteinsdóttir and Abdallah S. Daar are also at the Dalla Lana School of Public Health, University of Toronto, Ontario, Canada. Tirso W. Saenz and Maria Carlota de Souza Paula are at the Centre for Sustainable Development, University of Brasilia, Brazil. Wen Ke and Lexuan Li are at the Institute of Policy and Management, Chinese Academy of Sciences, Beijing, China. Magdy A. Madkour is at the Arid Lands Agricultural Research Institute, Ain Shams University, Cairo, Egypt. Sahar Aly and Nefertiti El-Nikhely are at the Center for Special Studies and Programs, Bibliotheca Alexandrina, Alexandria, Egypt. Sachin Chaturvedi is at the Research and Information System for Developing Countries, India. Victor Konde is at the University of Zambia, Lusaka, Zambia. e-mail: halla.thorsteinsdottir@mrcglobal.org*

and increased global trade<sup>2</sup>. Furthermore, developing countries have been setting up mechanisms to encourage increased trade with one another by establishing free trade zones, such as the Association of Southeast Asian Nations Free Trade Area, the Southern Common Market (Mercosur/Mercosul) in Latin America and the Common Market for Eastern and Southern Africa.

Developing countries have also been targeting science and technology sectors as key areas for encouraging South-South collaboration and are forging a growing number of bilateral, multilateral and regional agreements with this aim<sup>3</sup>. South Africa and Malawi, for example, have formed an agreement directed at accelerating economic growth and reducing poverty through the adoption of current global technologies<sup>4</sup>. In addition, there are significant science and technology components in regional collaboration efforts in developed countries, such as those organized by the New Partnership for Africa's Development (<http://www.nepad.org/>), and the IBSA network organized by India, Brazil and South Africa (<http://www.ibsa-trilateral.org/>). Health biotech provides a substantial scope for collaboration between developing



Members of the team studying South-South entrepreneurial collaboration in health biotech. From left to right: Sachin Chaturvedi, May Sanaee, Magdy A Madkour, Wen Ke, Halla Thorsteinsdottir, Victor Konde, Tirso W Saenz, Monali Ray, Christina Melon, Nefertiti El-Nikhely, Heba Maram.

countries as several developing countries have built up capacity in the field, including private-sector development<sup>5-9</sup>.

At the same time, analysts have called for increased South-South collaboration to address shared health problems<sup>10</sup>. Developing countries are increasingly aware of the importance of doing so through joint efforts with one another, and they have set up networks to deal with malaria, tuberculosis, HIV/AIDS and other common diseases. Together with Russia and the Ukraine, Brazil, China, Cuba, Nigeria and Thailand are working together in a network that jointly promotes research and development (R&D) aimed at developing innovative diagnostics kits, drugs and vaccines for HIV/AIDS prevention and treatment<sup>11</sup>. In addition, 24 manufacturers of vaccines in develop-

**Table 1** Number of health biotech firms surveyed and their response rates

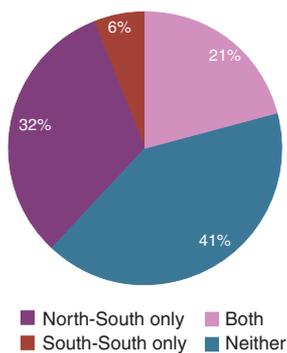
Country	Number of firms surveyed	Number of responses	Response rate
Brazil	110	72	66%
China	139	83	60%
Cuba	11	8	73%
Egypt	22	15	68%
India	121	68	56%
South Africa	64	42	66%
Total	467	288	62%

ing countries have come together to form the Developing Countries Vaccine Manufacturers Network (<http://www.dcvmn.com/>), which ensures a consistent and sustainable supply of quality vaccines to developing countries at an affordable price and encourages R&D efforts to meet the emerging vaccine needs in the developing world.

Although South-South collaboration in science and technology has been high on developing countries' agenda since the 1960s<sup>12</sup>, there is only a limited amount of empirical evidence that examines these collaborations. In health biotech, for example, we are not aware of any work confirming that developing countries' firms have heeded the call for South-South collaboration, or that they are to any significant degree working together. In this article, we aim to fill this knowledge gap and provide empirical data on South-South collaboration. We refer to partnerships between health biotech firms in developing countries (that is, low- and middle-income countries) as 'South-South firm collaboration'. Collaboration between firms in developing and developed countries (high-income countries) is called 'South-North firm collaboration'.

**Rationale for South-South collaboration**

One reason why firms in health biotech, both in developing countries and elsewhere, may want



**Figure 1** Extent of international collaboration of health biotech firms in developing countries and comparisons of their South-South versus South-North collaborations.

to work together is to minimize costs and risk. The commercialization of new health products and services in biotech is characterized by high costs and high risks<sup>13</sup>. Even though preclinical work may produce promising medicines, attrition of products remains high, with many lead candidates rejected after costly clinical human testing.

Another reason why collaborations are attractive is that they provide a conduit to new and foreign markets. Alliances between firms are often necessary to expand their markets<sup>14</sup>. Firms in small countries are particularly dependent on exporting their products to survive, and collaborative arrangements with firms in other countries are typically needed to obtain this access.

A third rationale for collaboration is to gain enhanced access to strategic knowledge or specific technical skills<sup>15-17</sup>. Both scientific and product development knowledge in health biotech is highly specialized, making it nearly impossible for small firms or institutions in developing countries to harness it all. Collaborations therefore become a means by which firms can obtain access to a wide spectrum of knowledge, technologies and skills, allowing them to implement new and relevant findings in their field. This knowledge can be requisite for various phases of health biotech development. For instance, for many small firms that are taking their first steps in product development, access to knowledge about regulatory authorities and processes in local and foreign markets is particularly important.

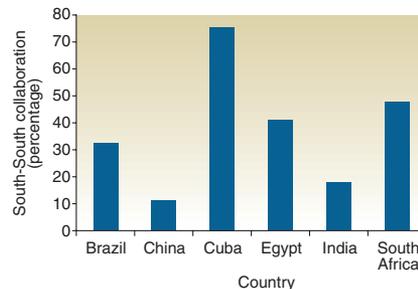
If developing countries can cultivate ways to work effectively together, they may be able to harness a more relevant model of promoting innovation than the traditional model of relying on linkages with developed countries. By pooling their expertise and resources, they could strengthen their capability to address shared problems—problems that may not affect the developed world nor capture the interest of companies there. If successful, South-South collaboration could increase capacity in science-intensive fields by allowing participants to learn from each other, improve the ability of developing countries to

address their own problems, and contribute to economic development and quality of life in developing countries.

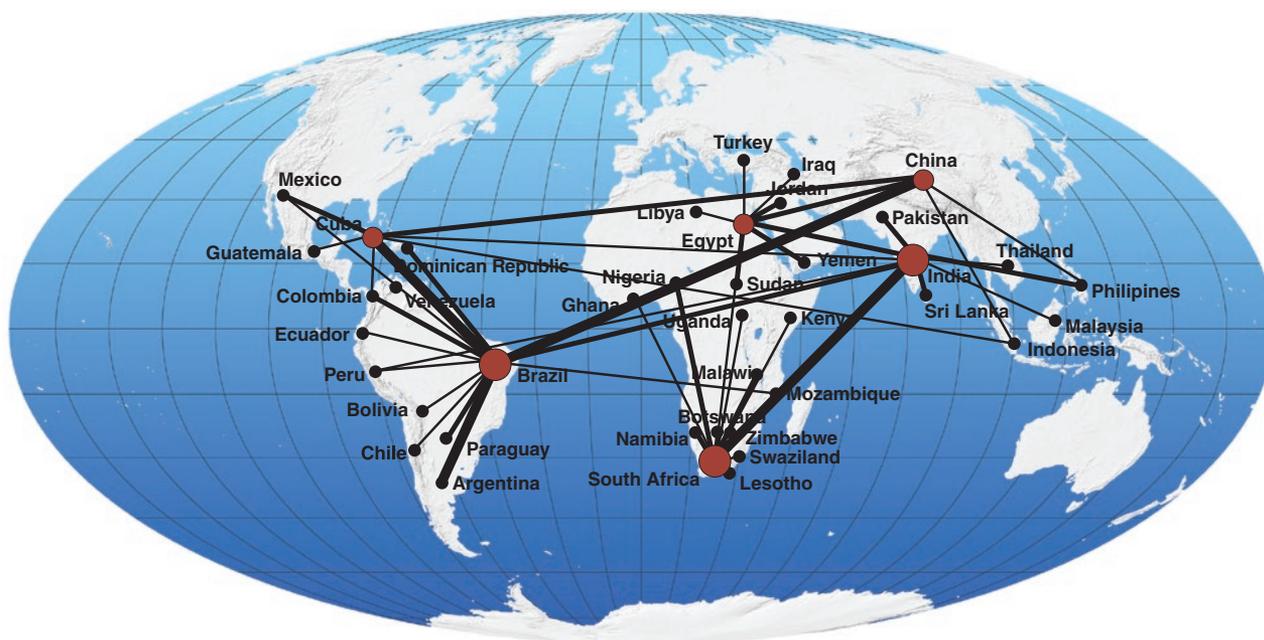
To examine the level and characteristics of South-South collaboration, we sent a brief survey to 467 health biotech firms in six developing countries that have relatively strong health biotech sectors—Brazil, China, Cuba, Egypt, India and South Africa—and asked about their linkages with all other developing countries. We selected these countries on the basis of our previous research identifying them as regional leaders in this field<sup>5</sup>. The survey was sent to all the dedicated biotech firms that we could identify in these countries, to pharmaceutical firms active in biotech and to other organizations heavily involved in commercialization activities in the health biotech field (see **Supplementary Methods** for a discussion on how we identified health biotech firms). We asked the firms whether they collaborated with firms or organizations in other low- and middle-income countries, and if so, to name their collaborators and provide an overview of each partnership. Data collected included the reasons for the collaboration, the activities involved and the output of the collaboration. We presented the firms with a broad definition of 'collaboration', including in that definition any work jointly undertaken by firms and organizations that contributes to the production of knowledge, products or services in health biotech.

A total of 288 firms completed the survey, a response rate of 62% (Table 1). We feel this is a solid response rate, given that participation was voluntary and the nature of the sector can make it challenging to get responses from firms. The sector is fluid, with companies frequently merging or going bankrupt. In biotech surveys by the Organisation for Economic Co-operation and Development (Paris) involving mandatory responses, only response rates under 50% are considered low<sup>18</sup>.

In the following sections, we describe the extent of South-South health biotech collaborations, map where the main linkages lie and



**Figure 2** Percentages of firms in the countries we surveyed that engage in South-South health biotech collaboration.



**Figure 3** Collaboration network of health biotech firms in South-South collaborations. The size of each node represents the total number of South-South collaborations for the country, while the width of each line represents the number of collaborations between the two linked countries. For clarity, only linkages of two or more collaborations were included on this map.

explore the main characteristics and outputs of the collaborations.

### Extent of South-South collaboration

The results show that South-South firm collaboration is substantial, with more than a quarter (27%) of the health biotech firms that responded reporting collaborations of this type (Fig. 1). South-North collaboration is still more predominant, however, with over half (53%) of the firms reporting collaborations with developed countries. A proportion of the firms in our sample (21%) indicated they engaged in both South-South and South-North collaborations.

We looked at the proportion of firms involved in South-South collaboration in each of the countries we studied (Fig. 2). Those countries in our sample with the smallest populations—Cuba and South Africa—are the most active in South-South collaborations, with almost half of the South African firms and three-quarters of the Cuban entrepreneurial organizations reporting involvement in this type of collaboration. This is in stark contrast to the more populated countries, such as China, where just over 10% of the firms report South-South collaborations, and India, with fewer than 20% of firms engaged in such partnerships.

According to our findings, almost all the countries studied are more active in South-North collaborations than South-South collaborations. Egypt was the only country that showed a lower rate of South-North collabora-

tion, with twice as many South-South collaborations as South-North (Table 2).

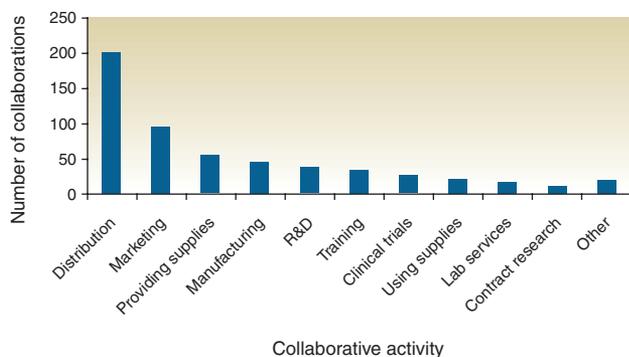
Most of the firms that are active in South-South collaboration are engaged in several collaboration initiatives. The total number of South-South collaborations reported in this study is 279. It is important to note, however, that some collaborations may have been double-counted; that is, a particular partnership between an Indian firm and a South African firm may have been counted twice—once for India and once for South Africa—if both firms responded to the survey and reported all of their collaborations. We attempted to address this issue by asking the respondents to provide the names of their partnering firms; however, many opted to keep this information confidential, thereby limiting our ability to adjust the number of collaborations accordingly. In such cases, the firms reported, for example, that they

collaborated with ‘firm A’ in India and ‘firm B’ in China. This may inflate the aggregate number of South-South collaborations.

On average, the firms reported taking part in 3.5 collaborations, with responses ranging from 2.8 collaborations per firm for Brazil to 5.7 collaborations for Cuba. Brazil has the largest number of South-South collaborations of the countries we surveyed, with well over 60 collaborations. Even though the countries with the smallest populations, Cuba and South Africa, have relatively low numbers of health biotech firms, they are so active in South-South collaborations that comparing their collaborations with those of large countries is still likely to produce valid results. South Africa has the second-highest number of collaborations of the countries in this study, and Cuba has slightly more collaborations than the population giant China.

**Table 2** Number of international collaborations reported

Country	South-South collaborations		North-South collaborations		Total collaborations	
	Number	Average number per company	Number	Average number per company	Number	Average number per company
Brazil	64	0.9	127	1.8	191	2.7
China	27	0.3	99	1.2	126	1.5
Cuba	34	4.3	63	7.9	97	12.1
Egypt	39	2.6	30	2.0	69	4.6
India	54	0.8	126	1.9	180	2.6
South Africa	61	1.5	66	1.6	127	3.0
Total	279	1.0	511	1.8	790	2.7



**Figure 4** Distribution of the activities involved in the South-South entrepreneurial collaborations for all the countries we surveyed.

We asked the firms to indicate who initiated the collaborations: themselves, their partners, government agencies, international organizations, expatriates or any other intermediary. Their answers indicate that the firms themselves typically initiated the collaborations. Governments or other local or international organizations seldom played this role, with only 17 of the 279 reported collaborations said to have been initiated by such organizations. Respondents from Cuba and Brazil were most likely to indicate governmental influence, typically targeting public research organizations that are heavily involved in entrepreneurial activities. Follow-up interviews in developing countries revealed that firms find it challenging to identify appropriate collaborative partners in other developing countries and to initiate the collaboration. Finding enough detailed information about potential partners is a difficult task, and building trust can also be challenging. Thus, there definitely is scope for governments and other third parties to take a more proactive role in initiating collaborations. It is also notable that only one of the collaborations was reported to be initiated by expatriates who have moved between the collaborating countries. One explanation for this may be a relatively low migration rate of professionals between developing countries. It would be interesting to see whether expatriates are more important in South-North health biotech collaboration.

In addition, we asked the respondents to indicate whether they had set up formal arrangements with their collaborators, and to elaborate on the nature of those arrangements where applicable. We found that most (almost 90%) of the collaborations involved at least one type of formal arrangement among participants, ranging from supply agreements to R&D cooperation agreements to marketing and distribution agreements. Licensing agreements were commonly cited, with around 19% of the collaborations having formal licensing contracts, whereas joint ventures were estab-

lished in only around 8% of the collaborations overall. South Africa (seven joint ventures) and Cuba (six joint ventures) had the highest numbers of joint ventures reported.

### Geography of collaborations

To map South-South collaborations in health biotech, we drew a diagram of the main linkages reported by the firms using the Ucinet 6 program (<http://www.analytictech.com/ucinet/>; Fig. 3). The countries we surveyed directly appear as hubs involved in various collaboration networks; it is not surprising that they are featured centrally. In contrast, this map is likely to under-represent the collaborations of countries we did not survey, such as Mexico, Nigeria and Malaysia. Nevertheless, the map provides an approximate overview of South-South collaboration in health biotech and shows that the strongest linkages of the countries we surveyed are with one another.

Chinese companies collaborate mainly with those in Brazil and India, Indian companies have close linkages with those in South Africa, and Brazilian companies have close linkages with firms in Cuba. The only other pairs of countries where companies are involved in a similar level of South-South collaboration are Brazil and Argentina, and South Africa and Botswana. As Argentina and Botswana are active in forming partnerships with other developing countries, surveying them would have provided an even fuller picture of South-South firm collaboration in this field. Our data, however, reinforces the notion that we surveyed the strongest countries in health biotech and that they collaborate with one another despite substantial distances.

The map of South-South collaborations also reflects the regional nature of health biotech partnerships between firms in developing countries. Every country in our survey has collaborations with other countries within its continent. For example, South Africa has numerous ties with other sub-Saharan coun-

tries, Egypt collaborates with Middle Eastern and North African countries, and there are many linkages of Brazil and Cuba with other Latin American countries.

### Characteristics of collaborations

To get a deeper understanding of South-South collaborations, we asked the firms what activities were involved in the collaborations, what were the reasons for partnering and what outputs had arisen from these deals.

**Collaborations involve mostly commercialization.** We asked the firms to specify the activities they were pursuing jointly in South-South collaborations, choosing from a wide selection of activities that are typically undertaken by health biotech firms, from research-intensive activities to end-stage commercialization activities such as distribution and marketing. We considered activities to be innovative if they focused on research and developmental activities of new products or services, or of production processes. This includes, for instance, clinical trials and laboratory services. Conversely, we regarded collaborations involving simply the packaging of products or their export between countries—that is, marketing and distribution—as noninnovative activities. We indicated to the firms that they should choose all the activities that were applicable to their collaborations, and we offered the option to add any other activities not included on our list.

The resulting responses show that the majority of the collaborations (60%) involve two or more activities. For example, rather than creating collaboration solely around distribution, partnership deals more usually involve distribution and another activity, such as providing supplies. It is also clear that most of the South-South collaborations involve end-stage commercialization activities, with around 200 (72%) involving distribution and 95 (34%) involving marketing activities (Fig. 4). Innovative activities were much less frequently cited by the firms that responded: R&D was part of only 36 (13%) of the collaborations, clinical trials just 25 (9%), and contract research only 9 (3%). It is noteworthy that the third most frequently cited collaboration activity was providing supplies, with 53 (19%) of the South-South collaborations involving such provisions. Supply activity can vary from providing plant material from which active pharmaceutical ingredients are derived for drug development to providing active pharmaceutical ingredients.

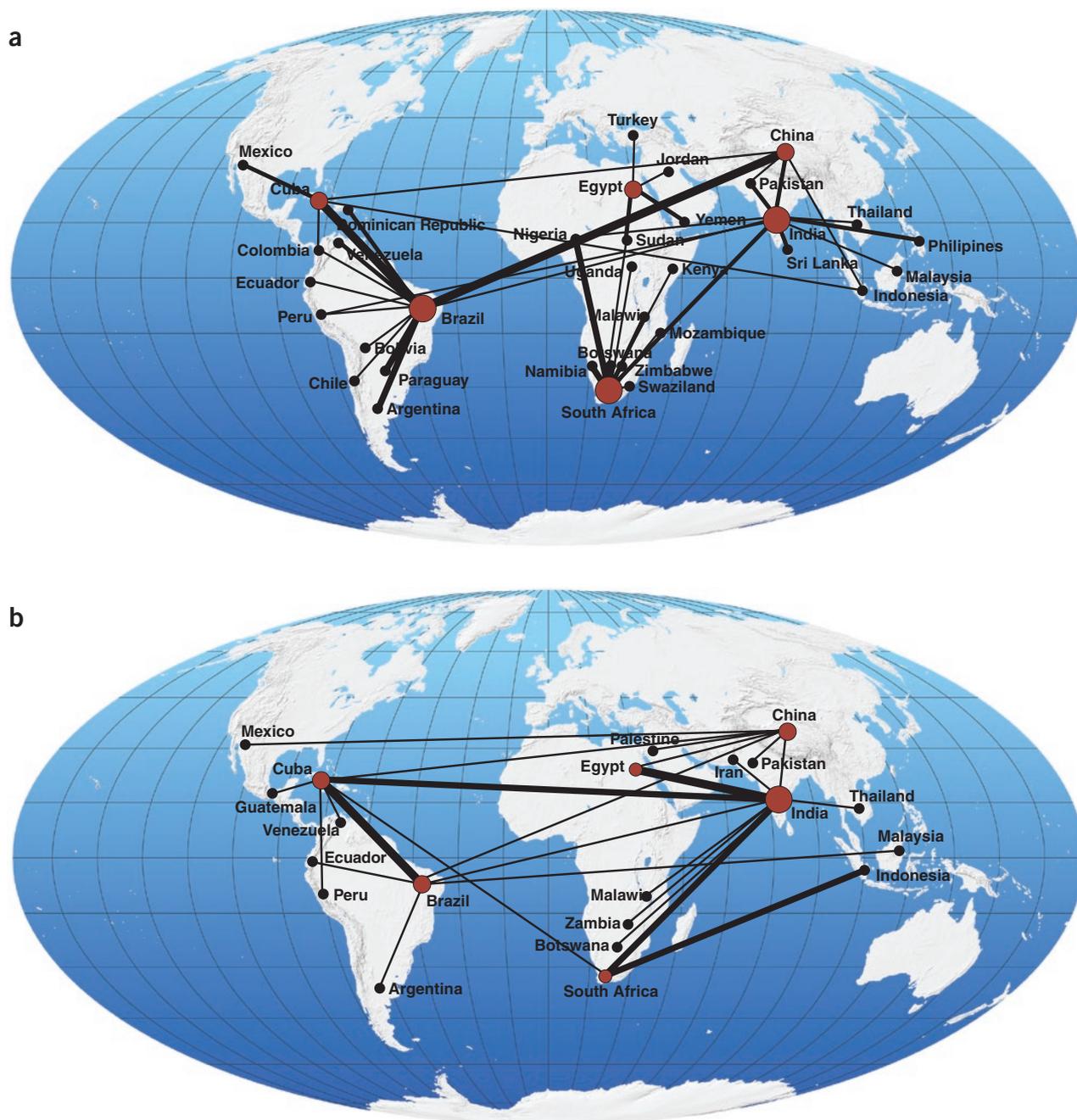
The relatively slight emphasis on R&D activities in South-South firm collaboration contrasts with that reported in an analysis

of North-North collaboration in biotech<sup>17</sup>. From the mid- to late 1990s, more than 20% of biotech collaborations between developed countries involved R&D, up from around 6% in the 1970s. It will be of interest to repeat this survey in a few years to detect whether R&D collaborations between developing countries also increase.

We then explored where the collaboration linkages lie for the different types of activities

(Fig. 5). Some of the activities represent only a few collaboration linkages, which certainly limits the possibility of generalizing from these results. As distribution and marketing are closely related activities, we graphed them together as 'end-stage commercialization'. There are relatively strong end-stage commercialization linkages between the leading developing countries in health biotech (Fig. 5a), with, for example, active distribution and

marketing collaborations between Brazil and China, Brazil and Cuba, India and China, and India and South Africa. They probably form linkages to reach each other's markets. Also striking are the widespread regional commercialization collaborations in health biotech. South African firms, for example, have distribution and marketing collaborations with well over 20 African countries, including relatively strong linkages with Botswana, Namibia and



**Figure 5** The network of collaborations involving end-stage commercialization versus R&D. (a) Collaborations involving end-stage commercialization. (b) Collaborations involving R&D. As in **Figure 3**, node size and line width denote numbers of collaborations. For clarity, only linkages of two or more distribution and marketing collaborations are included in **a**; all of the linkages are shown in **b**.

### Box 1 Vaccines for Africa's meningitis belt

To counter a meningitis outbreak in 2007 in the so-called 'meningitis belt' of Africa, the World Health Organization (WHO) decided to assess the status and production capacity of polysaccharide manufacturers worldwide. This assessment identified Bio-Manguinhos (Rio de Janeiro), in collaboration with the Finlay Institute (Havana), as the most suitable suppliers. Through South-South collaboration, they could quickly provide the needed products to address the outbreak at a lower price than that of alternative suppliers.

The meningitis belt in Africa stretches across the continent from Senegal in the west to Ethiopia in the east and covers several low-income countries with an estimated population of ~300 million. Samples from meningitis-infected individuals showed that the cases were caused by *Neisseria meningitidis* serogroup A, which is the most common serogroup in Africa but exists in neither Brazil nor Cuba.

The Finlay Institute has a long history of meningitis research and managed to control a meningitis outbreak in Cuba in the mid-1980s, developing a purified meningococci vaccine that was the first of its kind worldwide. Bio-Manguinhos also has extensive experience in vaccine research and manufacturing, and has developed an efficient scale-up process using lyophilization. By collaborating and relying on their respective strengths, these two organizations were able to supply, in a timely fashion, a meningitis A vaccine capable of combating the African meningitis outbreak.

For its part, the WHO also facilitated the collaboration by making it possible for ANVISA, the regulatory agency in Brazil, to collaborate with the Cuban regulatory agency CECMED. The agencies were able to exchange information about their respective regulatory systems, which made it possible for them to align the collaborative process. Neither Bio-Manguinhos nor the Finlay Institute alone would have been able to respond so quickly and efficiently to this request. This example therefore demonstrates how South-South collaboration can be harnessed to address a health threat when spurred by demand and funding from an international organization. It also shows how South-South collaboration can contribute toward improving global health (<http://www.who.int/mediacentre/news/notes/2007/np12/en/index.html>).

Indonesia. Firms in Cuba, India and China also have a few R&D collaborations with companies in other countries; in the case of Cuba, these are mostly regional collaborations with other Latin American countries, whereas India's collaborations are cross-continental and involve companies in several African countries. In addition, it is notable that China and India seem to be more heavily involved in collaborations surrounding end-stage commercialization and than in R&D partnerships.

Developing countries conduct joint R&D for several types of products. Vaccines are key to preventative health care in developing countries, and by working together on shared health problems, companies in the South can strengthen their potential for developing cost-effective products. Cholera is a shared health problem in Bangladesh and eastern India. The International Centre for Diarrhoeal Disease Research (Dhaka, Bangladesh) has been conducting leading research on cholera vaccine candidates, and its collaboration with the Indian firm Biological E (Hyderabad, India) has facilitated further the development of a cholera vaccine candidate. If the vaccine originating from the institute in Bangladesh proves efficacious and safe, the partners can gear up toward manufacturing of the vaccine by the Indian firm. Another example of vaccine R&D involves the Bio-Manguinhos (Rio de Janeiro) in collaboration with the Finlay Institute (Havana). These two institutions exploited each other's respective strengths to develop and manufacture a bivalent meningitis AC vaccine to address a meningitis outbreak in Africa (Box 1). This is a good example of how developing countries can use their assets in biotech to address health problems of other countries in need. And these types of collaborations extend beyond vaccines to more experimental types of therapy. For example, the South African firm Altis Biologics (Pretoria, South Africa) is partnered with the First Affiliated Hospital of Xinjiang Medical University (Xinjiang, China), which is carrying out animal testing of Altis's allogeneic human bone extract enriched in bone morphogenetic proteins, intended for use in implants for complex fractures and bone disease.

Although our survey results indicate that South-South collaborations rarely include clinical trials (another developmental activity), there are some interesting exceptions. Of the countries we examined, Cuba seems to have the greatest number of active clinical trial collaborations. Some of these collaborations involved South-South-North collaborations. CIMAB (the entrepreneurial arm of the Cuban Institute Center of Molecular Immunology; Havana), with its partner YM BioSciences (Mississauga, Canada), has spearheaded the establishment

Nigeria. Egypt has distribution and marketing collaborations with around 10 African countries and widely within the Middle East. India has commercialization collaborations with other Asian countries, such as Sri Lanka and Pakistan. Brazil has a relatively large number of commercialization collaborations with other Latin American countries, and it should be noted that its only commercialization collaborations in Africa are with Portuguese-speaking countries such as Angola and Mozambique. According to our survey, Brazil and South Africa do not have distribution and marketing linkages in health biotech with each other, nor do Egypt and South Africa.

We further found that China has frequent collaborations with both India and Brazil in providing supplies. It is also notable that South Africa mainly provides supplies to other sub-Saharan countries. This may indicate that its collaborations are focused on providing necessary products or ingredients for biotech development, including active pharmaceutical ingredients, to countries with limited capacity in this field. Our follow-up case study research has supported this notion.

The survey data suggest that India and China are most active in manufacturing collaborations, which is not surprising, as manufactur-

ing in general is an area of strength for both countries<sup>19–21</sup>. Their manufacturing collaborations appear mainly to be intercontinental, between the leading developing countries, with relatively strong ties between China and Brazil, India and South Africa, and India and Egypt. The large markets in China and India are attractive to companies in smaller countries, and this leads these firms to create Chinese and Indian joint ventures allowing local manufacture, thereby facilitating market entry and reducing the cost of transportation from the smaller country.

**R&D collaborations are limited and center around a few countries.** It is obvious from Figure 5b that R&D collaborations are not nearly as numerous as end-stage commercialization collaborations. The main linkages in R&D are between firms in the leading developing countries in health biotech. Most of these partnerships are between companies in Brazil and Cuba, India and Egypt, Cuba and India, and India and South Africa. An exception is collaborations between companies in Cuba and India, which seem to be relatively strong in R&D compared with end-stage commercialization. Other active R&D linkages were found between enterprises in South Africa and

of a global clinical consortium to test cancer therapeutics that are based on innovation from Cuba (Box 2). The network includes partners from 20 developing countries and thus has a heavy emphasis on South-South collaboration. China is also involved in South-South collaboration focused on clinical trials. For instance, the Chinese firm SH-IDEA Pharmaceutical Company (Yuxi, China) and the Kunming Institute of Botany (Kunming, China) are working with Thailand's Ministry of Public Health (Bangkok) on clinical trials of an HIV/AIDS treatment (Box 3). The study stems from original research from the Kunming Institute of Botany based on Chinese traditional medicine and local biodiversity, but the clinical trials were carried out on Thai patients.

It should also be noted that according to our survey, the South-South collaboration of Indian firms in clinical trials is limited. As India is known for active international collaborations involving clinical trials<sup>20–22</sup>, its lack of clinical trial partnerships with other developing countries perhaps reflects the greater allure of relationships with multinational pharmaceutical firms or with developed countries.

**Bidirectional knowledge flow is an important reason for collaboration.** To better understand the motivations for South-South firm collaboration, we asked respondents to indicate the reasons for each of their collaborations. Again, we note the multifaceted nature of South-South collaborations, with respondents reporting several reasons for single collaborations. In line with the heavy emphasis on end-stage commercialization, 'access to markets' was the main reason given for the collaborations (207 or 74% of the collaborations). It was an important reason for commercial collaborations in all the countries we surveyed; firms in developing countries are clearly working together to gain export markets for their products and services. The second most commonly cited reason for the collaborations was to 'provide knowledge' (72 or 26%), followed by 'gain knowledge' (52 or 19%). A relatively high proportion of Cuban respondents (68%) cited 'provide knowledge' as a reason for the collaboration. Brazilians also cited this reason fairly often, but they more frequently than the Cubans reported knowledge gain as a reason for their collaborations.

There is mention of clinical access as a reason, with 'access to patients' stated for 28 (10%) of the collaborations, mainly by Chinese and Cuban respondents. Finally, 'provide patients' was a factor in 13 (5%) of the reported collaborations. What is notable is how infrequently financial reasons were given for the collaborations, with 'access to financing' cited as a reason for only 15 (5%) of the collaborations,

and 'provide financing' cited only four times (1%). Cubans stood out again in citing 'access to financing' relatively frequently as a reason for their collaborations, as well as 'provide technology/equipment'. This may indicate that they have collaborations that involve licensing access to their technologies to other developing countries.

It is noteworthy how frequently 'provide knowledge' and 'gain knowledge' are cited as reasons for collaborations, especially given how rarely activities related to R&D were reported in our study. It points to a strong capacity-

building role for the collaborations, as seen in examples of technology-transfer initiatives (Box 4). This may mean that South-South collaboration is still in its infancy, though its aim is future knowledge-generation activities. The discrepancy may also reflect the different types of knowledge that are required in health biotech. South-South collaboration may be used to gain access to knowledge about each other's markets, to deal with regulatory affairs, and so on.

Some of the reasons reported here align well with reasons attributed to North-North or North-South collaborations<sup>13–17,23</sup>. Access

## Box 2 Global South-South-North consortium for clinical trials

To carry out cost-effective clinical trials, CIMAB, the commercial arm of Cuba's Center of Molecular Immunology (Havana), and its partner YM BioSciences (Mississauga, Canada), have established a consortium of firms around the world for testing the humanized monoclonal antibody nimotuzumab in the treatment and diagnosis of patients with cancers of epithelial origin. The consortium (<http://www.ymbiosciences.com/products/nimotuzumab/codevelopment.php>) has partners from 20 developing countries as well as 7 developed countries, including Argentina, Brazil, Colombia, Mexico, Peru, Paraguay and Uruguay from Latin America, Algeria, Egypt, Morocco, Nigeria and South Africa from Africa, and China, India, Indonesia, Malaysia, Pakistan and the Philippines from Asia. Asia is especially strong in the consortium, with Japan, Singapore and South Korea as developed-country participants. Other high-income countries in the network are Saudi Arabia and Germany. The consortium thus reflects a South-South-North collaboration with strong participation from developing countries. Examples of southern firms in the consortium are Biocon Biopharmaceuticals (Bangalore, India), Biotech Pharmaceutical Co. (Beijing), Eurofarma (Sao Paulo, Brazil) and Laboratorios PiSA (Guadalajara, Mexico)

Nimotuzumab is a Cuban innovation from the Center of Molecular Immunology that targets epidermal growth factor receptor. It is aimed at various epithelial cancer types, including non-small cell lung, glioma, esophageal, brain metastasis, colorectal, pancreatic, prostate, cervical and breast cancers. To date, the consortium has tested nimotuzumab in 9,842 patients in Cuba, Argentina, Brazil, Canada, China, Colombia, Germany, India, Indonesia, Japan, Malaysia, Mexico, Singapore, South Africa, South Korea, Thailand and the Philippines. Trials are also being conducted in Europe, Japan and North America. CIMAB and YM BioSciences work to ensure that the network of firms follows the regulatory guidelines of the International Committee for Harmonization/Good Clinical Practice. The consortium's clinical trial results are collected in a central depository. Aggregating patient data from sites in the various countries increases the statistical power and quality of the clinical trials. By amassing data gathered under internationally recognized norms from the collaborating sites, the partners are able to submit a stronger drug application to their national regulatory authorities. Gaining approval from one regulatory agency can pave the way for other agencies to be able to approve the product. Currently, nimotuzumab has been approved for marketing as a treatment for head and neck cancers and glioma in 23 countries worldwide, including Argentina, Brazil, China, India, Indonesia, Mexico and Ukraine. The consortium members license the drug from CIMAB and market it in their home countries.

Running clinical trials in developing countries among several partners has a number of advantages. Economies are obtained through the lower personnel and infrastructure costs and by sharing clinical trial expenses across several partners. Patient recruitment is faster, even for rare cancer indications, owing to the large patient populations, who previously lacked access to treatments. Thus, not only are costs reduced, but trials are completed at a faster pace. The example of nimotuzumab shows that a consortium of enterprises consisting primarily of small biotech firms from developing countries can complete these studies at the same speed as, and at lower cost than, big pharma. By including a South-South collaboration strategy, biotech firms have an alternative to partnering with pharma companies in clinical development and can potentially retain greater presence in the later stages of a product's development and a greater share of revenue stream.

to markets and knowledge are both consistent incentives. Even so, given the findings from developed countries, where the need to access financing and minimize costs regularly stimulates collaboration, we expected access to financing to be cited more often as a reason for South-South collaborations than we found. We therefore cannot conclude that the South-South collaborations were fuelled by motivations to minimize costs.

**Collaborations are strongly product focused.** We asked the respondents of the survey to report the outputs of their South-South collaborations. The majority of collaborations, roughly 65%, have resulted in some specific output. The collaborations are strongly product focused, with 70 (25%) collaborations leading to a joint product in the market and 16 (6%) leading to a joint product in the pipeline. Thus, these types of partnerships facilitate the end-stage commercialization of health biotech products produced by firms in developing countries and increase the availability of these products in developing countries.

Even so, very few collaborations result in the joint development of products; instead, these

types of commercial relationships are confined to licensing arrangements. Thus, only 16 (6%) collaborations led to joint products in the pipeline, and joint patents were reported as an outcome for only 12 (4%) of the collaborations. Cuban and Brazilian enterprises were the only ones that reported joint patenting as an outcome of their collaborations. Not surprisingly, South-South firm collaboration seems to rarely result in joint publications of a scientific paper (reported only once as an output of collaboration). Other reported outputs included the following: clinical/scientific research results, human resource training, separate product development, and technology transfers.

Our analysis also reveals that more than half of partnerships involving R&D had joint products on the market, and a quarter of them had joint products in the pipeline. Even though there is generally a limited emphasis on product development in the South-South collaborations examined here, product development and end-stage commercialization activities are closely linked. Several developing countries are currently signatories of the TRIPS (trade-related aspects of intellectual property rights) agreement, and firms in these countries have started

to place an increasing emphasis on R&D and developing 'new to the world' innovation<sup>6,24,25</sup>. Our survey results suggest that those firms may be relying, in part, on their commercialization linkages with other developing countries to jointly strengthen their R&D activities. This is a promising sign that South-South collaborations will, in the future, become important in strengthening health biotech innovation within developing countries.

## Conclusions

Our analysis indicates that South-South entrepreneurial collaboration in health biotech is substantial and that firms in developing countries are actively working together. These types of collaborations are on the political agenda of many developing countries' governments, and, as mentioned above, developing countries are increasingly signing collaborative agreements and setting up initiatives to promote scientific and technological collaboration among themselves. Our results show that in the health biotech sector, at least, firms have moved beyond the rhetoric of South-South collaboration. They are actively boosting trade in their countries by forming relationships with firms in other developing economies; to a lesser degree, they are working together to boost innovation, as seen in the development of new products or processes.

Apart from providing insight into the current extent and characteristics of South-South collaboration, our survey also establishes a baseline for future studies. As such, it can provide important information for evaluating the effects of policies and programs aiming to promote collaboration in developing countries. As with any survey, our study has limitations. For logistical reasons, we had to limit our data collection to a few countries—those that are likely to contain the bulk of developing countries' firms active in this field. Furthermore, we have not been able to receive information from every firm active in health biotech in the countries we focused on, and some firms may not have reported the extent and characteristics of all their South-South collaborations. Even so, as we obtained a relatively high response rate, we believe that the results represent the main characteristics of South-South firm collaboration in the health biotech field.

In summary, our findings lead us to several conclusions. First, we can see that South-South collaboration has become a widely chosen path for health biotech firms. One in every four firms that responded to our survey stated an active collaboration with other developing countries. Furthermore, developing countries' firms that engage in South-South collaboration are likely to be involved in several initiatives at a given

### Box 3 A South-South approach to dealing with HIV/AIDs based on local biodiversity

China and Thailand are working together to develop a remedy against HIV/AIDs based on Chinese biodiversity and knowledge from traditional Chinese medicine. The collaboration involves both public and private-sector institutions. The start of a collaboration between the two neighbors was marked in 1997, when a memorandum of understanding was signed by their ministries of public health. As a part of this collaboration, an official partnership was established between the Department of Medical Science within Thailand's Ministry of Public Health (Bangkok) and the Kunming Institute of Botany (Kunming, China) of the Chinese Academy of Sciences (<http://stats.yuxi.gov.cn/showitem.asp?id=2006120717303184815>).

Thailand has a higher reported prevalence of HIV/AIDs than China, making it a preferred partner for China. The Thai government was highly motivated to address the rising health threat of HIV/AIDs, and its larger patient base facilitated clinical trial testing. Interest in this collaboration was spurred by a visit of Thai officials to the lab of Luo Shide at the Kunming Institute. In the late 1990s, Shide had carried out a series of experiments analyzing *ex vivo* the pharmacological and toxicological properties of a mixture of flavones and triterpenoids with inhibitory activity against HIV protease and reverse transcriptase, originally purified from a Chinese traditional remedy, Ke' Aite. After initiation of the collaboration, a team of researchers in Thailand repeated the preclinical work in preparation for the commencement of clinical trials. To scale up and manufacture the therapeutic candidate, the two groups struck up a collaboration with the Chinese firm SH-IDEA Pharmaceutical Company (Yuxi, China). The resulting product—Complex SH—is the first herbal-based anti-HIV drug to have undergone phase 1, 2 and 3 testing in China and Thailand<sup>28</sup>. The product is patented and has received regulatory approval in both China and Thailand.

In light of controversy over the pricing and availability in developing countries of small-molecule inhibitors of HIV protease and reverse transcriptase marketed by Western drug companies, it is noteworthy that South-South collaboration can harness an alternative solution to address a local health threat. This example also shows how governmental will can cultivate South-South collaboration, enabling two countries to develop a therapeutic based on knowledge from the South.

time. South-South collaboration has therefore become a reality of the health biotech sector—a well-trodden route firms take in their entrepreneurial activities. Nonetheless, South-North collaborations are even more prevalent, with just over one in every two firms being active in collaboration with at least one developed country. There were also differences in the extent of South-South entrepreneurial health biotech collaborations depending on the location; countries with the smallest populations were most active in collaborating with other developing countries. This probably reflects the fact that small home markets can create the need to collaborate for the sake of a firm's viability.

Second, this survey shows that most collaborations involve linkages between the leading developing countries in health biotech. Despite distances, working together may amplify the competitiveness of relatively advanced developing countries. In addition, the results show a considerable number of regional collaborations between firms. Firms in South Africa, for example, have active linkages with other sub-Saharan countries, and enterprises in both Brazil and Cuba had active collaborations in Latin America. Thus, South-South collaborations have a dual purpose: to amplify the global competitiveness of leading developing countries in health biotech and to strengthen regional ties in health biotech.

Third, the health biotech collaborations between developing countries involve mainly end-stage commercialization activities rather than R&D. Commercialization activities such as distribution and marketing were by far the most common South-South collaboration activities, and more common than any research and developmental activities. This is true for all the countries surveyed in this study. The focus on end-stage commercialization is in line with 'access to markets' being the most common reason given for South-South collaborations and reflects a need for companies to export their products to other developing countries. The fact that the countries with the smallest populations were most active in South-South collaborations underscores this finding. Considering that some developing countries have proven track records in producing relatively affordable health biotech products<sup>26</sup>, South-South health biotech partnerships may increase the availability of relatively inexpensive health biotech products in developing countries' markets, as well as the accessibility of health biotechnologies in general.

Fourth, these collaborations contribute only marginally to innovation in health biotech. Few of the South-South collaborations reported in the survey involved knowledge-creation activi-

#### Box 4 Extending health biotech capacity through South-South collaboration

Technology transfer features centrally in South-South collaboration in health biotech and can lead to substantial capacity building in countries that lack technological proficiency in certain areas. In one example, an Egyptian company has forged collaboration with a Chinese firm to enable the production of recombinant insulin in Egypt, which was previously imported and as a result was often in short supply in the Middle Eastern country. The partnership involved the transfer of technology to produce recombinant insulin from the Chinese company Dongbao (Shanghai) to the Holding Company for Biological Products and Vaccines (VACSERA) in Giza, Egypt. As a result, Egypt now has a facility that can produce recombinant insulin locally, and diabetics in the country have a reliable and readily accessible supply of insulin that is cheaper than the imported product. The technology transfer from China has thus considerably benefitted the Egyptian health system. As economic and political turmoil can lead to an unsteady supply of important health products, self-sufficiency is far from being a trivial goal for developing countries.

Elsewhere, India has transferred technology for diagnosing infectious diseases to South Africa. East Coast Rapid Diagnostics (now split into Tulip South Africa and Life Assay, both of Durban, South Africa) is a joint venture between the publicly funded LIFE labs in South Africa (Durban) and the Indian Tulip Group Diagnostics (Bambolim, India). Under the agreement, the Indian company transfers several diagnostic technologies to South Africa, including rapid malaria diagnostic kits and pregnancy diagnostic kits, together with substantial capacity and technical assistance. These diagnostic kits are stable at high temperatures and are thus suitable for application in Africa, where cooling can be hard to achieve in supply chains. In return for the technology transfer, LIFE labs will commercialize and market the kits in other African countries with high incidences of malaria and other infectious diseases.

These two examples show that South-South technology transfer can lead to a stronger supply of essential health products in developing countries, more affordable than the imported alternatives and well-adapted to the needs of local populations. Such collaborations are thus a cost-effective and efficient way of promoting global health.

ties tied to innovation. For example, only 13% of the reported collaborations involve R&D and only 9% involve clinical trials. This may indicate that many of the firms we surveyed are not active in health biotech innovation. Instead, they may be licensing products from firms that are innovators in the field—typically from developed countries. Nevertheless, some firms from China, Cuba and India have increasingly been applying their innovative capabilities to the health biotech field<sup>5–7</sup>. It will be of interest to repeat the survey in the future to see whether South-South collaboration will make a richer contribution toward innovation. It is also notable that collaboration involving R&D activities has a strong commercial side, with 'joint product on market' being the most frequently cited output for the R&D collaborations. This reflects the sizable product focus of R&D collaborations, which may translate into a stronger innovation track record once more firms have been able to build up innovation capacity.

Fifth, South-South collaboration is typically initiated by the participating firms themselves. The results of the survey show that little collaboration has been initiated by governmental organizations or by any other outside party;

international organizations and expatriates have also had a limited role in encouraging South-South collaborations. As research on South-North collaboration between firms has suggested that a major challenge of health biotech collaboration is establishing the initial linkages with possible collaborators<sup>27</sup>, it seems likely that this challenge is also experienced by the firms of developing countries. Our results may indicate an opportunity for greater governmental involvement. The example of the Brazil-Cuba collaboration on meningitis AC vaccine for Africa exemplifies the important role that international organizations can play in facilitating South-South collaboration. The involvement of other international organizations or philanthropic organizations might also be warranted to accelerate the formation of collaborations that provide affordable options for improving health in developing countries.

On the basis of our research, we can make several recommendations. Firms in developing countries should consider South-South collaboration as a way to expand their markets. Market demand has been expanding in many developing countries, and it is thus an increasingly lucrative strategy to target those markets<sup>2</sup>. Setting up a collaboration with a firm

in another developing country that has knowledge of the local regulations relating to product quality and product manufacture, as well as an established product distribution network, is an important first step toward accessing these markets. Firms in developing countries should realize that by working together they can leverage each other's strengths and develop more cost-effective products. In doing so, they can expand their markets considerably in the developing world, where a large proportion of the population can afford only low-priced health products. Firms in developing countries can start their cooperation by focusing on marketing and distribution, but as their collaboration deepens and trust is built, they can start to pursue further innovative activities with commercial partners.

Governments in developing countries should continue to place an emphasis on South-South collaboration. As more developing countries have built up capacity in health biotech, they now can use collaboration with other developing countries to build capacity in areas where knowledge is lacking. Technology transfer between developing countries can be a promising strategy to gain access to technologies that are typically more affordable and appropriate to developing countries' needs than the technologies from developed countries. Such collaborations can strengthen the capacity of firms based in countries currently weak in health biotech and can start bridging the divides between developing countries in this field.

Our survey also shows that even though South-South firm collaborations in health biotech are widespread and numerous, they rarely involve innovation. Developing countries are not yet reaping the full benefits of such commercial partnerships. With an increased innovation focus, developing countries could leverage their individual strengths and increase the pool of resources to address their shared problems. We thus recommend that governments in developing countries integrate South-South collaboration more closely in their innovation policies and provide support to firms from other developing countries that want to promote joint innovation in health biotech. To smooth the process of innovation, these governments may need to consider how their regulatory offices can work together to make the process of cross-border innovation easier and faster.

Finally, our survey shows that governments and international organizations have had a

limited role in initiating South-South collaboration. Promoting a stronger innovation focus in South-South health biotech collaborations should not be dependent solely on the activities of enterprises in developing countries; supportive activities that directly target the development of health biotech products and services are called for from both governments in developing countries and the international community. International organizations and philanthropic organizations that are engaged in promoting global health should pay attention to the power of South-South commercial collaborations in providing affordable health products. When health biotech firms in developing countries pool their respective strengths, there is potential for such collaborative efforts to be more cost effective and relevant than the work of health biotech companies in developed countries; thus, South-South collaborations may be able to provide health products that reach more poor people in the developing world.

*Note: Supplementary information is available on the Nature Biotechnology website.*

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#### COMPETING FINANCIAL INTERESTS

The authors declare competing financial interests: details accompany the full-text HTML version of the paper at <http://www.nature.com/naturebiotechnology/>.

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