S1 (box) | METHODS

The research reported in this paper is based on two large scale research projects. In these projects we examined North-South and South-South collaboration in the field of health biotechnology. Both research collaboration (mainly between researchers at universities and public research organizations), and entrepreneurial collaboration (mainly between private sector firms) were studied. We relied on quantitative as well as qualitative methodologies to carry out our research; scientometric analysis of co-publications, surveys of firms and case study research were conducted to study international health biotechnology collaboration. To carry out the scientometric analysis we collaborated with the firm Science-Metrix (Montréal, Canada) that has specialised in scientometric analysis. To carry out case study research on South-South collaboration in health biotechnology we collaborated with groups in five developing countries. They are from the: Centre for Sustainable Development, University of Brasilia (Brasilia, Brazil); Institute of Policy and Management, Chinese Academy of Sciences (Beijing, China); Arid Lands Agricultural Research Institute, Ain Shams University (Cairo, Egypt); Center for Special Studies and Programs (CSSP), Bibliotheca Alexandrina (Alexandrina, Egypt); Research and Information System for Developing Countries (New Delhi, India); and University of Zambia (Lusaka, Zambia).

Mapping scientific collaboration

We mapped Canada-developing countries scientific collaboration as well as research collaboration between developing countries. This was done through scientometric analysis of health biotechnology publications, where co-publications of authors in different countries were used as a proxy for their collaborations.

To gather scientometric data we used the Elsevier Scopus database and a subset of all papers published in the 1996-2009 period that fall within the field of ‘health biotechnology’. Scopus has a broad coverage of natural and social science literature, including more than 15 000 peer-reviewed journals from over 4000 international publishers. Scopus makes it possible to identify papers that are co-authored by researchers from institutions in different countries, by linking all the authors of papers to their institutional addresses. Although Scopus lists several types of documents, only articles, notes, reviews, and conference proceedings were retained in producing the scientometric indicators as they constitute a core medium for information diffusion. In addition, they all have been through the peer review process ensuring that the research constitutes an original contribution to scientific knowledge.

This scientometric analysis is based on a set of papers from Scopus that fall within the field of biotechnology. Biotechnology papers were retrieved from the Scopus database using keyword-in-title searches to specifically select biotechnology papers. The keywords were selected as follows: firstly, papers were randomly selected from journals specializing in biotechnology; keywords and keyword combinations were then chosen from the titles of these papers in order to retrieve other papers in the field of biotechnology. Subsequently, subsets of papers were constructed from the biotechnology dataset to delineate the domains of health biotechnology.
To classify the papers into subfields of health biotechnology we used the National Science Foundation’s (NSF) classification scheme applied in its Science and Engineering Indicators series (see: http://www.nsf.gov/statistics/seind06/). We retained only biotechnology papers published in journals classified in any of the three following fields of science: biomedical research, clinical medicine, and the health sciences. Of these, papers published in the 1996–2009 period were retained.

Addresses from the papers were standardized according to country. The World Bank’s classification of countries was used; we defined developing countries as those that are classified as low and middle income countries by the World Bank. In our North-South study we focused particularly on papers that Canada has co-authored with authors from developing countries. In the South-South study we examined co-authored papers of authors from two or more developing countries. We considered statistics including the numbers of papers in health biotechnology written by authors in our focus countries (Number of papers). We examined the papers published by researchers in these countries in collaboration with developing countries colleagues (International collaboration). We considered the relative importance of international collaboration in a country by dividing the country’s number of papers written in collaboration with other countries, by the country’s total number of papers in health biotechnology (Collaboration rate) and looked at the pattern of collaboration over time and in terms of geographic distribution (Network of collaboration). We also examined the subfields of health biotechnology that most frequently involved international collaboration. The scientometric analysis enabled us to determine the most active developing country collaborators of our focal countries for further study as explained below.

Mapping firm collaboration

To examine the level and characteristics of Canada-developing countries firm collaboration in health biotechnology, and also of entrepreneurial collaboration between developing countries, we carried out surveys of health biotechnology firms. In one study we sent a brief survey to 259 health biotechnology firms in Canada and asked the firms about their collaborations with low and middle income countries. In the other study we sent the survey to 467 firms in Brazil, China, Cuba, Egypt, India and South Africa (developing countries that have relatively strong health biotechnology sectors) and asked them about their linkages with all other low and middle income economies. We followed a broad definition of ‘collaboration’, considering it to be any work jointly undertaken by firms and organizations in developing countries that contributes to the production of knowledge, products or services in health biotechnology.

Health biotechnology firms in Canada were identified using the BioteCanada, Industry Canada and Contact Canada databases. Firms in these databases self-identify themselves as working in the health biotechnology sector. We first combined these databases. Then we collected additional information about each firm on the greater list from their websites. To identify health biotechnology firms in the selected countries, we referred to biotechnology industry association databases, such as ABLE (Association of Biotechnology Led Enterprises) in India, and other official lists of biotechnology firms in the countries we studied. We also included a few public sector organisations as a part of our survey, that are known to be active in entrepreneurial
biotechnology, particularly from Brazil and Cuba. We collected additional information on the types of biotechnology in which each firm engages – primarily from company websites and publicly-available literature. Based on this information, we removed firms that did not seem to be active in the health biotechnology field such as those involved in agri-biotechnology, veterinary biotechnology, industrial biotechnology, environmental biotechnology, biofuels, cosmetics, consulting and investment. Firms that remained on our list included those involved in biopharmaceuticals, pharmaceuticals, diagnostics, bioinformatics, regenerative medicine, laboratory services, clinical trials, contract research, natural remedies and nutraceuticals. Consensus had to be reached between three members of our team in determining whether a firm was removed or remained on the list.

We sent the surveys on international collaborations to the CEOs and Heads of Research & Development and/or Partnership Development of the health biotechnology firms, as well as other organizations heavily involved in entrepreneurial activities. To encourage a good response rate the survey questionnaire was kept brief, asking a total of ten questions (for list of questions, see Box 1). When they were engaged in collaboration with developing countries, we gathered additional information on the country and/or firm name(s) as well as the activities involved, the reasons for the collaborations, the output of the collaborations, who initiated the collaboration, etc. We first administered the survey questionnaire via an online survey service called Instant Survey, to make it easier for the firms to respond. We later made extensive follow-up calls to non-respondents. Firms were then sent their responses for verification. In a few cases, responses from recent in-depth interviews with members of our research team were used in lieu of a survey response.

**Box 1 Survey Questions**

1. Does your firm collaborate or work together in any way with firms or organizations in developing countries?
   *Choices:* Yes or No

2. If ‘YES’, please list the collaboration initiative by presenting the name and location of the partner firm/organization (e.g. ABC Inc., China).

3. What activities do each of the collaborations entail?
   *Choices:* R&D, Contract research, Laboratory services, Clinical trials, Manufacturing, Providing supplies, Using supplies, Distribution, Marketing, Training, Other (please specify).

4. What are the reasons for the collaborations?
   *Choices:* Access to markets, Gain knowledge, Access to technologies/equipment, Access to patients, Access to financing, Provide markets, Provide knowledge, Provide technologies/equipment, Provide patient access, Provide financing, Other (please specify).

5. What types of technologies does each of the collaborations involve?
   *Choices:* Vaccines, Biopharmaceuticals, Diagnostics, Pharmaceuticals, Drug delivery systems, Herbal medicines, Equipment/devices, Drug delivery systems,
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Bioinformatics, Other (please specify).

6. What type of partner organization(s) is/are your firm cooperating with?
   Choices: Firm, Research institute, University, Hospital, Government, Other (please specify).

7. What types of formal arrangements have your firm established with your collaborator(s)?
   Choices: Joint venture, Licensing agreement, Strategic alliance, Subsidiary, Memorandum of understanding, Other (please specify).

8. What types of outputs have each of the collaborations produced?
   Choices: Joint product on market, Joint product in pipeline, Joint patent, Joint publication, Other (please specify).

9. Who initiated the collaboration?
   Choices: Your firm, Partners in developing countries, Your government agency, Your partner’s government agency, International organization, Expatriates, Other (please specify).

10. Does your firm collaborate with firms or organizations in industrialised/high income countries? Please see [World Bank link] for the list of countries that fall into this category.
    Choices: Yes or No

In Table 1 we indicate the number of responses and response rates we achieved from health biotechnology firms surveyed in the countries of our focus. Overall, of 726 firms we sent our survey to, we received 469 responses.
Table 1. Number of health biotechnology firms surveyed and their response rates

| Country   | Number of firms surveyed | Number of responses | Response rate (%) |
|-----------|--------------------------|---------------------|-------------------|
| Canada    | 259                      | 181                 | 70                |
| 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                |

Our analysis examined the extent of entrepreneurial collaboration Canada, Brazil, China, Cuba, Egypt, India and South Africa have with southern partners. We further looked at several characteristics of the collaboration including the distribution of the activities involved in the South-South collaboration, the reasons for the collaboration and what outputs the collaborations had lead to.

**Case study research on North-South and South-South collaboration in health biotechnology**

We then carried out case study research to examine further the potential for Canada’s collaboration with developing countries and South-South collaborations in health biotechnology. We identified the main drivers for the collaborations, the challenges the collaborations have met, the impacts of the collaboration and examined what can be done to strengthen the international collaborations. Our focus was both on research collaborations as well as entrepreneurial collaborations in order to gain a broad perspective.

The decision was to base the case study data collection on existing health biotechnology collaborations to learn from researchers and entrepreneurs that have had direct experiences in either Canada-developing countries collaboration or South-South collaborations. To identify which countries were the main collaborators of our focal countries we relied on our mapping of scientific and firm collaborations. The mapping exercises enabled us to identify where research and entrepreneurial collaborations were strongest, and use that to guide our decisions on which linkages to examine in more detail.

The countries examined in this research were:
Canada’s collaboration with Brazil, China, Cuba, India, Peru, Tunisia
Brazil’s collaboration with Argentina and Cuba
China’s collaboration with India, Thailand and Cuba
Egypt’s collaboration with China and Jordan
India’s collaboration with Brazil and Bangladesh
South Africa’s collaboration with Kenya and Zambia
Sub-Saharan Africa’s (i.e. Kenya, Nigeria and South Africa) collaboration with China and India

The identification of research collaborations relied on the results from the mapping of research collaborations. From the list of collaborations generated this way, we chose collaborative papers to examine for each of the focal countries. For each paper we
interviewed scientists from the specific developing countries of interest that had co-authored the paper in question and/or their collaborators in the other country. We asked them about the collaboration carried out to produce the papers and learned from them about the potential, challenges and impacts of the collaborations.

The identification of entrepreneurial collaborations for further analysis was based on the results of mapping entrepreneurial collaborations. Generating these lists of collaborations helped us identify potential entrepreneurial collaborations on which we could focus. From these, we interviewed entrepreneurs from the specific developing countries of interest and their collaborators in the other country. We asked them about their entrepreneurial collaborations and learned from them about the potential, challenges and impacts of the collaborations.

In each country we also interviewed other members of the local health biotechnology innovations systems to gain better insights into the policies and programs that are in place to promote South-South collaboration, and how both the regulatory and intellectual property systems impact the South-South collaboration in health biotechnology and their innovations.

Most of the interviews were carried out in face-to-face settings. They were either carried out in the local language or English. Where consent to be voice recorded was granted, the interviews were recorded digitally. When interviewees consented to their participation, but not to being voice recorded, notes were hand-written in lieu of recording audio. The audio files from the recorded interviews were transcribed and analyzed using content analysis. The analysis of the case studies will combine descriptive quantitative indicators gleaned from the documents with the in-depth qualitative analysis of the documents and interviews. A total of 506 interviewees were conducted in the 16 countries (Table 2).

Additionally, we collected extensive background information on the specific cases of collaborations we elected to focus on by examining the research papers, joint patents, and other outcomes that resulted from the collaboration. We also examined, where available, the annual reports from the firms involved in the collaborations, and collected government reports and other governmental documentation such as policy briefs; descriptions of existing policies, priorities, and initiatives; and legal and regulatory arrangements. Content from the websites of institutions and/or firms also served to supplement the other data sources.
Table 2. Number of interviewees in the different countries interviewed for case study research

| Countries               | Number of interviewees |
|-------------------------|-------------------------|
| **Canada study**        |                         |
| Canada                  | 79                      |
| Brazil                  | 27                      |
| China                   | 32                      |
| Cuba*                   | 7                       |
| India                   | 26                      |
| Peru                    | 13                      |
| Tunisia                 | 4                       |
| **Brazil study**        |                         |
| Brazil                  | 15                      |
| Argentina               | 17                      |
| Cuba                    | 10                      |
| **China study**         |                         |
| China                   | 20                      |
| India                   | 9                       |
| Thailand                | 6                       |
| Cuba                    | 3                       |
| **Egypt study**         |                         |
| Egypt                   | 34                      |
| China                   | 16                      |
| Jordan                  | 28                      |
| **India study**         |                         |
| India                   | 24                      |
| Brazil                  | 18                      |
| Bangladesh              | 8                       |
| **South Africa study**  |                         |
| South Africa            | 27                      |
| Kenya                   | 10                      |
| Zambia                  | 10                      |
| **Sub Sahara Africa study** |                     |
| Nigeria                 | 22                      |
| Kenya                   | 16                      |
| South Africa            | 25                      |
| **TOTAL**               | **506**                 |