The Institute for Medical Biology (IMB), located in Singapore’s sprawling Biopolis, is one of a handful of research organizations generated in a global mission to understand and treat human disease. Kristin Kain investigates.

The Institute for Medical Biology’s (IMB’s) mantra is ‘building bridges between basic science and clinical medicine.’ “Everybody [at the IMB] is working on something targeted toward understanding mechanisms of human disease or projects that we hope will lead to strategies for dealing with disease,” says IMB director, Birgit Lane. To do this, the IMB intends to reach into the medical community and pull human health issues from their identification ground in the clinic back to the bench. In the laboratory, research scientists within the IMB can lend mechanistic insight to pathological processes and identify useful areas that might advance disease diagnosis or treatment. “One of the biggest challenges is: how do you encourage collaborations between basic scientists and clinicians when they have a different way of working, they have a different set of priorities and different agendas? And yet, the scientists really need the input and experience of the clinicians in order to make sure the research is going in the right direction, and the clinicians need to work with the scientists in order to make this research happen in a meaningful way for clinical work.” The communication circuitry necessary for these collaborations includes medics, pharmaceutical companies and basic science researchers with a common drive to promote human health. Thus, the IMB encourages interaction between researchers at the bench and patient oriented clinicians allowing a stream of ideas and information to flow in both directions.

As a new research institute, established in April 2007, the IMB faces a special challenge in recruiting the best scientists to approach its mission. The IMB’s location is fundamental to its strategy and its ability to succeed at the interface of research and medicine. It requires an environment that facilitates the interaction of scientists with clinicians and pharmaceutical companies. Thus, the unique community surrounding the IMB is of particular importance.

The IMB is nestled within Biopolis (Fig. 1), a large research and technical center comprising nine buildings and 2 million square feet just west of the southern tip of Singapore. It shares its status as an A*STAR (Agency for Science, Technology and Research) institute with six others within Biopolis, which cover areas of shared interest such as genomics, bioinformatics, biomedicine and bioprocessing. There is an “undercurrent of translational thinking,” says Lane, “common to all the institutes within A*STAR”. All A*STAR institutes also focus on training, so providing access to graduate students and postdoctoral scientists is certainly one draw when recruiting senior scientists. As Sai Kiang Lim, a Principal Investigator at the IMB, notes, “IMB has all the attractions of working at an A*STAR institute in Biopolis: generous funding, superb infrastructure and state of the art supporting technology platforms.” An additional major advantage of all of these institutes is that they are government funded, freeing scientists from the invisible chains that would likely otherwise tie them to a reliable stream of grant writing. Lane highlights that “to have a government that is seriously trying to adequately fund biomedical research is a real treat. I don’t suppose I’ll ever experience that again and it’s great to be here and to be a part of it”.

In its effort to stimulate the exchange of ideas, Biopolis brings scientists with training and expertise in different fields together and creates an environment to promote their interaction. The complex provides a home for five research consortia and private tenants, including the pharmaceutical and drug development companies, Novartis,
Lilley and Schering Plough, in addition to the seven A*STAR institutes. To facilitate the flow of research from their institutes to medical application, Biopolis offers support with industrial development and technology transfer. They provide access to an experimental therapeutics center to interface between research discovery and drug development. Cafes, shops, exercise facilities, shared meeting rooms, common lecture halls and outreach programs of cross-over interests are located on site to create a ‘work, live, play’ environment aimed to promote interaction among its tenants. Many of the buildings are also attached through a series of sky bridges where people can flow from one section to another.

To complement the exchange of ideas that takes place within Biopolis, the complex sits within a larger Singaporean community, which is scientifically and medically rich. Within a few minutes drive, Biopolis members can find themselves at the National University of Singapore, National University Hospital or the National Skin Center. Fostering extensions into these groups and nearby clinics is another way to increase awareness of clinical needs among the research community at the IMB. Laboratory heads at the IMB are encouraged to establish external collaborations. Alan Colman, made famous by his participation in the cloning project of Dolly the sheep, is the executive director of the Singapore Stem Cell Consortium as well as a Principal Investigator at the IMB. The Consortium’s goal is to “bring together people who have interests in stem cell research throughout Singapore… including people in universities and hospitals,” notes Lane and this will stimulate collaboration. Lane has set another example for promoting community interaction by pioneering the Skin Club, which is a reflection of the commonality between her research interests in skin and in skin fragility diseases and the work of the National Skin Center of Singapore’s dermatologists. She points out that the success of these groups is dependent on their accessibility to everyone. For that reason, the Skin Club has meetings in the early evening when most members can attend. A typical meeting includes two talks, one by a clinician and one by a scientist, to encourage the two groups to interact and make it clear that everyone’s unique perspective is valued. She commented that, “This has actually stimulated two or three very solid collaborations that I know about and it has introduced a lot of people to each other. It really is an approach that works.”

Singapore’s commitment to being an international leader in science and medicine is clear after investing US$500 million (US$365 million, €235 million) toward the Biopolis structure and continuing to dedicate significant funds to support its scientists. Ironically, the autocratic government style that facilitated the efficient genesis of Biopolis without challenge and the birth of the IMB only 12 months after its approval, could also pose a threat to recruiting the most prominent international scientists that they seek, since scientists can greatly value their independence and autonomy.

However, Singapore boasts many features that may prove attractive to international scientists, including a tropical climate with moderately warm temperatures year-round, and a reputation for being a clean and safe city. In addition, English is an official language making Singapore accessible to many Western scientists. Numerous resources are available for expatriates, including associations representing most international groups, help for relocation, rental services and organized social events involving locals and other expatriates. There is even a monthly magazine committed to ensuring that expatriates make the most of Singapore. Singapore is a relatively small city-state surrounded by narrow straits, but it is located relatively close to choice travel destinations such as Bali, Thailand, Borneo, Indonesia, New Zealand and Australia. Thus, Singapore offers an experience and a different way of life that may appeal to adventurous scientists (Fig. 2).

In this unique environment, the IMB celebrated its inception just over a year ago. It has managed to attract a number of noteworthy scientists, including 15 group leaders across a wide spectrum of age and nationalities, many of whom are international luminaries. In the area of stem cells, a major focus of the institute, Alan Coleman has drawn in groups working on how to turn stem cells into useful and safe tissue cells. One team’s studies focus on the creation of insulin-producing stem cells, a vision that Coleman hopes will someday lead to the treatment of diabetics who currently rely on constant blood monitoring and insulin shots. Other teams work on generating heart muscle cells, or neuronal stem cells as useful therapeutic tools. In another approach, Sai Kiang Lim has been using products secreted from partially differentiated mesenchymal cells to promote growth and regeneration in damaged tissues, such as ischemic areas in the heart resulting from myocardial infarction. The

Fig. 2. Singapore’s amenable tropical location is a draw for many scientists. Courtesy of Philip Ingham.
recent addition of the eminent developmental biologist Davor Solter, best known for his work on early developmental processes in the embryo, brings in another complementary dimension to this stem cell work.

Cancer research at the IMB is currently led by the groups set up by Françoise Thierry and Axel Ullrich. Recent great strides in cancer treatment have been due in part to Ullrich’s efforts in uncovering the roles for aberrant signaling through protein tyrosine kinases during cancer development and progression. New chemotherapeutic drugs, such as the multikinase inhibitor Sutent, which Axel Ullrich helped to develop, are now being used to successfully treat cancer patients. As a senior consultant, Ullrich still continues to bring valuable lessons from this drug development success to Singapore. Thierry’s research on viral proteins identified the role of the human papillomavirus (HPV) E2 proteins in cervical cell transformation during the genesis of cervical cancer. She also has been actively involved in live virus vaccine development and sees a unique opportunity for prophylactic vaccine development as an anti-cancer drug. She expects her appointment at the IMB to facilitate this work because, “collaboration with other groups in IMB will help us develop an in vitro model for HPV infection to study the influence of viral proteins on cellular transformation and differentiation.”

Genetic disease is another focus at the IMB and Birgit Lane receives international respect for her work describing the role of keratins in skin fragility disorders such as epidermolysis bullosa simplex (EBS) and pachyonychia congenita (PC), which cause epidermal blistering and hyperkeratosis. In addition to this work with skin diseases, she is beginning to uncover the relationships between keratin mutations and a patient’s predisposition to other diseases, such as liver cirrhosis and pancreatitis. Colin Stewart, a recent recruit from the National Cancer Institute at Frederick, MD in the USA, is studying the mechanisms that lead to premature ageing in another gene cluster, which is associated with disease arising from nuclear envelope mutations. In addition, Bruno Reversade is pioneering our understanding of the genetic events that allow for the occurrence of human twins, which should provide insight into the genetic and epigenetic mechanisms that underlie natural cloning events – leading back to the stem cells research programs.

Lane points out that a common goal of these diverse projects is their translational potential, “We are thinking both in terms of translation from basic science to clinical work as well as basic science into commercial application.” The IMB has carved a niche within a large and prosperous medical research community where its own internal interactions should find synergy. Bolstered by government support and proximity to a diverse medical and research community, the IMB continues to expand on the success of Biopolis, as demonstrated by the influx of top scientists. However, time will reveal both the strengths and weaknesses of this novel approach to translational research. The most important benchmark will be its ability to convert innovative science into better patient care.