Medtech Insight

Pharma intelligence | informa

Your complimentary Medtech Insight content

Medtech Insight
Pharma intelligence | informa

From Small Republics Big Ideas Grow

By Tina Tan, 30 Aug 2016

IN A BID TO EXPAND THE talent pool in its burgeoning medtech sector, Singapore has looked to the US West Coast – long regarded as a leading innovation hub in the global medtech arena – for ways to nurture a new generation of commercial-minded innovators. One such initiative is the Singapore-Stanford Biodesign (SSB) program, modelled after the renowned and successful Biodesign program at Stanford University. Tina Tan spoke to Ruey Feng Peh, director of SSB, to find out more about the program and what its outcomes have been to date.

• • •

It may be the Asian way, but Ruey Feng Peh appears unduly modest about the achievements of Singapore-Stanford Biodesign (SSB), the innovation training program that he has been involved in pioneering since its inception in 2010.

The key aim of the initiative – modelled after the Stanford Biodesign program launched in 2000 in the US that Peh graduated from as a fellow in 2008/2009 – is to train and nurture the local talent pool to become the next generation of medical device innovators, both in Singapore and Asia.

On returning to Singapore after his time at Stanford, Peh joined the Agency for Science, Technology and Research (A*STAR), the country's lead public sector agency that spearheads economic-oriented research to advance scientific discovery and develop innovative technology. He became part of the team to help strengthen Singapore's growing medical device industry. "The medtech landscape in Singapore has mainly been about downstream activities, manufacturing, sales and marketing, and post-product services – not a lot in innovation," he told *Medtech Insight*. "But we know we have very good engineers; we have a very strong engineering base in Singapore and we have invested heavily in the biomedical sector, so the biomedical foundation is strong."

Shutterstock: Kanuman

Singapore Seeks To Be Fertile Source Of Medtech Innovators

Having considered different innovation training programs from across the world, the Singapore government decided to adopt the Biodesign model from Stanford, which was "one of the first few institutions that champions innovating from an unmet needs perspective first," said Peh.

While there is a genre of innovation that is focused on "technology push" – "come up with something clever, something cool, then figure out what this solution could solve" – the innovation process that founding members of Stanford Biodesign (notably Paul Yock and Josh Makower) have come up with is based heavily on design-thinking principles.

"You start the process from being very clear about what the clinical need is, [then] you launch yourself into a

Reprinted by Medtech Insight (medtech.pharmamedtechbi.com). Unauthorized photocopying prohibited.

brainstorm to find what the solution is – agnostic to the technology – to fit that need. That is the mantra we started in Stanford, and we've brought that methodology in Singapore," Singapore-Stanford Biodesign's Ruey Feng Peh says.

Now, nearly six years after SSB was launched, the program has trained more than 320 individuals through its core fellowship program, through the classes and workshops it runs at the country's major universities, and through its corporate membership program.

And during this time, work by SSB fellows and students have led to the filing of more than 22 patents, while seven projects have attracted more than S$3.5m ($2.6m) in grants and other public funding. Upon seeing such momentum, Peh and his team created the Fellowship Extension program and internal runways to allow SSB talent and staff to advance their projects in-house more intentionally. Within three years after the launch of this initiative, two of these seven projects have progressed to become start-ups – Advent Access and Privi Medical.

As a comparison, Stanford Biodesign has spun off an impressive 39 companies over the 16 years since it started. But it may not be altogether fair to compare the US program with its Singapore counterpart. After all, Stanford Biodesign is set amidst an environment with a far longer history of medtech innovation and a more mature infrastructure to support this. What SSB has achieved to date would be deemed respectable by many, considering that the small Southeast Asian republic only really began stepping-up its investment to stimulate R&D in the life sciences, including biomedical sciences, in the last 25 years or so. (Also see " Singapore Moves Upstream In The Medtech Value Chain " - Medtech Insight, 20 May, 2016.) Singapore's medtech ecosystem – albeit growing at a significant pace – is still not as established as other regions, such as the US and Europe.

Source: A*STAR

Ruey Feng Peh, program director, Singapore-Stanford Biodesign

"You start the process from being very clear about what the clinical need is, validate that there is indeed that pain point, and be able to discern and characterize that pain point into a need. Then you launch yourself into a brainstorm to find what the solution is – agnostic to the technology – to fit that need. That is the mantra we started in Stanford, and we've brought that methodology to Singapore." Singapore-Stanford Biodesign's Ruey Feng Peh says.

The ways in which SSB alumni have made an impact on the medtech ecosystem are varied. Aside from those that have gone on to start companies that develop new technologies, there are physicians who have gone back to practicing medicine, but now invent and encourage innovation.

Peh conceded that Singapore is not yet near the level of innovation seen in the "medtech Mecca" that is the US West Coast, and he told *Medtech Insight* that "it will be very difficult to match the output of Stanford." However, he maintained that creating start-ups was not set as a key performance indicator for SSB when the program was launched – the fact that the program has already led to two start-ups being formed was a bonus, he said. "We measure ourselves by the number of people we train, and of the people we train, we see if they go on to make an impact on the medtech ecosystem," explained Peh.

The ways in which SSB alumni have made an impact on the medtech ecosystem are varied. Aside from those that have gone on to start companies that develop new

Reprinted by Medtech Insight (medtech.pharmamedtechbi.com). Unauthorized photocopying prohibited.

technologies, there are physicians (SSB selects fellows from multiple disciplines, including those from a medical/engineering/design/commercial background) who have gone back to practicing medicine, but now invent and encourage innovation. One example is an SSB fellow who was an urologist at Singapore General Hospital, and after graduating from SSB, he went to on to start a device development office within the hospital that brought together physicians and engineers to incubate ideas from scratch.

Additionally, SSB has been a source of talent for the existing multinational companies that have set up shop in Singapore. Examples include a fellow who already had industry experience, but after the program that person was hired by another medtech multinational to start its first R&D center outside of the US. Another SSB fellow also went on to join the M&A department of a company, applying her knowledge of identifying promising innovation to select potential targets to buy.

Six years into SSB, there has also been some tweaking of the original methodology that was brought over from the US. "When we first started, we took the entire process from Stanford Biodesign, but now we're starting to see some differences emerge," said Peh.

Many of these differences are seen in the third and final phase of the innovation process: "Implementation." (The first and second phases are "Identify" [clinical need] and "Invention," respectively). "In the Implementation phase, we are seeing more features emerge which are unique to the different geographies. The way IP is regulated or enforced in [the US vs Asia], the reimbursement landscape, the regulatory strategy. As the Singapore arm of Stanford Biodesign, we have taken some baby steps [in identifying these geographic idiosyncrasies]. We're putting together a list of how things might be different when launching products from Asia, or for Asia, for example."

In addition, SSB has expanded the clinical immersion phase of its fellowship program to the wider Asian region. Clinical immersion occurs during the needs identification stage, when fellows are immersed in the clinical environment and have a "fly-on-the-wall" perspective of what goes on in the hospital. During clinical immersion, fellows have access to different parts of the hospital and have the opportunity interview doctors, nurses and patients. The goal is to identify at least 300 clinical needs in a particular clinical space that they have been assigned; for example, ophthalmology.

Singapore is seen as the gateway to Asia, and SSB is keen to leverage this proximity to the largest market in the world in terms of population size, said Peh. "We want our SSB fellows to not just do the clinical immersion in Stanford or in Singapore, so we're now sending them to hospitals in the wider Asian region. We could be one of the first innovators to identify and address clinical needs that may have been overlooked by Western communities."

Many of SSB's recent fellows have done their clinical immersion in Indonesia, which Peh believes could be a sleeping giant behind India and China. "It's an interesting, emerging market and we are working with the hospitals there to learn about their needs." SSB also has a partnership in Korea, although the focus of that collaboration is more strategic. "We're helping Korea start its own Biodesign program there and in return, they help us understand the intricate details of entering the Korean market. Together, we explore co-innovation opportunities."

According to Peh, SSB is but one component of Singapore's developing medtech ecosystem. But its role is an important one: supply talent. And that talent, trained to be "savvy" to what true innovation is, should contribute to the wider goal of Singapore gaining recognition as a world-class health-care innovator.

From the editors of Clinica

Reprinted by Medtech Insight (medtech.pharmamedtechbi.com). Unauthorized photocopying prohibited.

SSB: A Springboard For Advent Access, Privi Medical

Since its inception in 2010, the Singapore-Stanford Biodesign innovation training program has led to the filing of more than 22 patents and seven publicly funded projects. Of these seven projects, two have progressed to become start-ups – Advent Access and Privi Medical.

Advent Access

Advent Access was founded and is now headed by Ruey Feng Peh, who was a Stanford Biodesign fellow and is currently program director for Singapore-Stanford Biodesign. The company's mission is to pioneer vascular access innovations to restore quality of life for kidney failure patients, and reduce the cost of dialysis in Asia and across the world.

According to Peh, the market for caring and managing kidney failure patients on hemodialysis is worth around $67bn today. However, up to a third of the costs of managing dialysis patients is not related to the dialysis technology itself, but to vascular access – specifically, access to a surgically created vessel, the arteriovenous fistula (AV fistula), which connects the artery and vein. It is this vascular access that allows the patient's blood to be removed, dialyzed and returned to the body.

The AV fistula is "a very precious, specially modified vein," said Peh, not only because it provides the lifeline for dialysis patients, but there are a limited number of sites where this fistula can be created.

However, for many years, the main way of accessing the AV fistula is by blindly sticking a needle into the patient in hopes of penetrating at the target spot. This inconsistent needling approach, which is highly operator-dependent, is not only painful for the patient, but exacerbates the wear and tear of the AV fistula. "These patients have to go through dialysis three times a week for generally four hours per session and they need two needles on their fistula each time. In literature, the average fistula lifespan is said to be about two to five years," said Peh. During this time, complications with the fistula can arise – a common one being aneurysms, another stenosis of the fistula – which require this vein to be repaired and ultimately be replaced by creating a new fistula, or switching to a synthetic AV graft, which has a shorter lifespan and a higher risk of complications.

"That's when the cost of maintaining these dialysis patients starts creeping up; when the fistula fails and you need to create another fistula or implant a graft through a repeat surgical procedure," Peh told *Medtech Insight*. "A lot of these complications could be preventable, as the frequent [and imprecise] needling cause weakness and injuries on the vein."

Many of the technologies in the area of vascular access for hemodialysis are looking at repair of the fistula, for example, angioplasty technologies, he said. "But not many are looking at preserving the fistula during its wear-and-tear phase. So Advent Access' technology is designed to delay the need for intervention and increase the longevity of the fistula." This will, he believes, ultimately lower costs and save the health-care payer money.

The *av-Guardian* by Advent Access comprises two implants made from medical grade titanium. These implants are designed to act as a "door" to the AV fistula. Each implant is placed subcutaneously on the "A" and "V" needle spots above the AV fistula, via a minimally invasive procedure. The implants are sutured to the skin for 14 days, after which the growth of tissue around the implants mean they should be "locked" into position naturally, and the sutures can be removed.

"We do a 'feel it, find it, follow it' technique. So the implant acts like a door that gives you access to the fistula. The caregiver will feel for the device [under the skin], have the needle penetrate the middle section of the device to find an inner lumen. Then you follow the lumen to guide the needle to the fistula," explained Peh. "So the needle will penetrate a specific part of the fistula, and the ability to penetrate the same spot of the fistula, at the same angle and at the same depth, allows a device-guided 'buttonhole track' to be formed over time."

This buttonhole track is effectively scarred-down tissue leading from under the skin to the fistula. When the

Reprinted by Medtech Insight (medtech.pharmamedtechbi.com). Unauthorized photocopying prohibited.

track is formed, a blunt needle can then be used to access the fistula instead, resulting in less trauma to the AV fistula and less pain for the patient when they are being hooked up for dialysis. "It's akin to creating a piercing in your earlobe to wear an earring, like creating a high-quality and predictable 'earring track' with the help of the av-Guardian device," said Peh.

This buttonhole technique is not altogether new and has been around since the 1970s. Medical literature comparing the use of buttonhole tracks for regular vascular access with other needling techniques have demonstrated that the buttonhole technique, when executed properly, can reduce many of the common complications with failing AV fistulas and also delay intervention. However, one significant barrier has been the high level of skill required to master the buttonhole technique in order to yield these advantages reliably. The av-Guardian allows this technique to be improved and standardized so anyone can be a skilled nurse, said Peh. By removing this skill obstacle, this could, he believes, potentially allow dialysis to be performed by non-professional caregivers and even by the patients themselves, disrupting the traditional hemodialysis care delivery model and opening up the market for home and in-center self-dialysis.

"Home hemodialysis is an emerging technology and trend, but its penetration of the market is still only 1 percent. It is well known that vascular access is the Achilles' heel of dialysis and makes it difficult to be performed outside the [medical] center, so we are the last piece of the puzzle. For in-center dialysis, we learned that the top technical obstacle preventing centers from setting up self-care stations to minimize cost, or opening twilight shifts with minimal nurse support to treat a larger patient pool, is vascular access."

Advent Access is in the midst of a small clinical trial at Singapore General Hospital and National University Hospital to validate the safety of the av-Guardian. The company has also initiated efforts to apply for CE-mark approval. "Our experience in our clinical study [so far] has given us valuable learning, and we are looking at preparing our pipeline and platform to enable in-center self-dialysis, to help dialysis centers to treat more patients, at a lower cost, with their existing machines."

The av-Guardian system: stencil plates, implants and delivery device

Source: Advent Access

Peh added: "We are learning that what we have invented at Advent Access could not only impact vascular health, but also disrupt the way dialysis can be scaled to meet here-and-now needs of dialysis centers."

Privi Medical

Privi Medical, currently in stealth mode, was founded by three of the four fellows who graduated from SSB in 2014. During the fellowship program, Privi's co-founders – Prusothman Raja, Benjamin Tee and Rena Dharmawan – were charged with identifying a clinical need within the gastrointestinal space and developing a solution to meet this need.

Having gone through the clinical immersion that is integral to the SSB program, and then whittled down the hundreds of needs that they identified, Raja told *Medtech Insight* that the one clinical need that emerged at the end of the filtering process was for a solution to treat lower-grade hemorrhoids.

"Hemorrhoids is so common; you'd see a case of hemorrhoids at least twice a day in the gastrointestinal space," he said. But while there are clinical interventions available to treat more severe, grades 3-4 hemorrhoids, the choice of treatment options for grades 1-2 hemorrhoids is very poor. "We first observed this

Reprinted by Medtech Insight (medtech.pharmamedtechbi.com). Unauthorized photocopying prohibited.

need in Stanford [Hospital, where we did part of the clinical immersion]. There, patients with grades 1-2 hemorrhoids were told to go home and nothing was given to the patient. They were just told to make some lifestyle changes – drink more water, eat better, try not to sit down for too long – and that's it."

With no real solution to relieve them of their symptoms, these patients' quality of life is significantly impacted. Additionally, the condition is a recurring one – sometimes as frequently as six to seven times a year in some cases, with each episode lasting one to two weeks – which further adds to the patient's distress.

The team therefore decided to develop a solution that could provide not only symptomatic relief, but also be drug-free so it addresses the concerns of pregnant women or new mothers, who make up a large proportion of hemorrhoid sufferers. "Some 80 percent of pregnant women develop haemorrhoids, and the patients we saw [during the clinical immersion] were new mothers. Most of them refuse to take any ointments or oral drugs for their hemorrhoids because they are worried about the effects of the active component in these products. So making our solution drug-free was among the early criteria we had set," said Raja.

Moreover, the team wanted to develop a device that can be used at home and self-administered by the patient. "The patients would be able to use this product to treat themselves at home without the doctor having to administer it. Also, with Asians [*the incidence of hemorrhoids is three times higher in Asia – Ed.*], they don't like going to the doctor repeatedly. The hemorrhoids bother them, but they would just tolerate it so they don't have to go to the doctor. So this is something that plays into our product," said Raja.

Being in stealth mode, the founders of Privi were not able to disclose the details of how their drug-free device works. However, Tee and Raja were able to tell *Medtech Insight* that it is a class I, single-use device, and the mechanism of action is one that is well known and, in scientific literature, has shown the ability to reduce symptoms of hemorrhoids.

Privi's technology has undergone proof-of-concept, and some animal and cadaver studies. The firm has to date received around S$0.5m of public and private funding, and is currently planning its first-in-man trial, with the possibility of gaining a CE mark and entering the market sometime in the second half of 2017.

From the editors of Clinica

SINGAPORE-STANFORD biodesign

Email: ssbenquiry@scei.a-star.edu.sg | **Phone:** +65-68172989 | **Website:** www.ssbiodesign.org