



# Biotech Daily's CEO interview

June 13, 2008

## HE'S THE BOSS: MESOBLAST'S PROF SILVIU ITESCU

The founder of New York's Angioblast Systems and Melbourne's Mesoblast, Prof Silviu Itescu is defensive about his ill-defined roles in the two companies.

The buck stops with him so he's the boss, but his various titles of founder, director and chief scientific adviser, don't define what he does.

From his office in a part of the Dick Pratt empire on the 39<sup>th</sup> floor of 55 Collins Street, Silviu Itescu has an excellent view of the world and he is clearly a man with great oversight as well as meticulous attention to detail.

Born in Ceausescu's Romania in 1957, Silviu's parents were sponsored to come to Australia when he was seven years old. He is measured in his assessment of Romania's dictator, who allowed Jews to leave the Iron Curtain - in exchange for cash payments.

Silviu followed a well-worn immigrant path, from Elwood Primary School to Caulfield North and then Melbourne High School, graduating in 1975 and taking a place at Monash Medical School the following year. He did a one year internship at the Alfred Hospital and that's where his trajectory differs from most.

Silviu's next job was a residency at New York's Bellevue Hospital, the public teaching hospital of the University of New York. Not a lot of second year-out doctors do that. The patients were the poor, the homeless, the huddled masses and Melbourne's Dr Itescu "arrived right in the middle of the AIDS epidemic".

"Thirty percent of admissions were HIV/AIDS patients," Silviu says.

So it wasn't a surprise that when he completed his residency he undertook a three year fellowship in immunology and rheumatology at New York University.

He says Bellevue Hospital residents were given a free rein, so there was a great deal of responsibility in decision-making. Most New York doctors can find somewhere more upmarket to practice. Doctors at the Bellevue were often there through choice.

In 2000, Dr Itescu was recruited to Columbia University, which had the biggest heart transplant group in the US, to establish an immunology research unit for transplants.

“We were looking for alternatives to transplants – it’s just not an option for most,” Silviu says. “There are 4,000 transplants in the US a year and 60,000 on the lists and many more who could have a transplant.”

He says there was the idea that if you couldn’t transplant the organ, then what about part of the organ?

“We were trying to grow tissue in the laboratory. They were already using bone marrow transplants. You build on other people’s work, nothing comes out of thin air,” Silviu says.

Using Federal Government grants, his unit at Columbia developed a method to proof-of-principle stage using adult bone marrow to grow heart muscle.

It led to recognition of the highest order - a paper in *Nature* in 2001, with the snappy title of ‘Neovascularization of ischemic myocardium by human bone-marrow-derived angioblasts prevents cardiomyocyte apoptosis, reduces remodeling and improves cardiac function’ (*Nature Med.* 7: 430-6 {2001}). Columbia’s director of transplantation immunology for the Departments of Surgery and Medicine had come a very long way in the 36 years since leaving Romania.

“We were using whole bone marrow. We didn’t quite know what to go after. And we never intended to commercialize it. Columbia encouraged us to set up Angioblast Systems.”

Along with seed investors, Columbia University, medical personnel and pharmaceutical executives the company was founded, but “the business model didn’t make sense”.

“We needed to move it to off-the-shelf cells for treatment,” Silviu says.

Angioblast continued its investigation of stem cells and biologicals for cardio-vascular disease. The core of the technology is manufacturing generic cells that can become cartilage, fat, bone or cardiac tissue.

Antibodies are used to identify specific cells which are extracted from bone marrow, then amplified into billions of cells. Importantly, they don’t activate the immune system. The cells left behind are the ones that trigger immune reactions.

“I don’t know why they don’t activate the immune system, but they don’t.” Silviu says disarmingly, his eyes full of a young scientist’s enthusiasm. “We got lucky.”

One leading Melbourne cardiologist, who owns shares in Mesoblast, says it is the only way forward. Transplants depend on dead donors and their numbers are insufficient. He says pumps won’t be favorable until they are small enough to fit into the body without any external wiring.

But the cardiologist also notes: “The issue will be how to effectively get enough new stem/heart muscle cells into the appropriate area efficiently in large enough numbers to do the job. So far, apart from direct injection at the time of cardiac surgery, other methods such as catheter-based techniques, which one would ultimately like to think would be the preferential way of cell introduction, have been proving not overly efficient.”

The search for a stem cell solution led to Adelaide's Hanson Institute, Medvet and Dr Paul Simmons. Angioblast had no interest in the orthopaedic program, but Silviu saw the value of having stem cells for both bone and cardiac.

"I set up Mesoblast in Australia specifically to commercialize the orthopaedic indications for the technology. Not too many start-ups can do both simultaneously."

Silviu had known Richard Pratt's son-in-law Alex Waislitz since university days and had acted as a biotechnology sector consultant to the Pratt family company, Thorney.

Silviu says he owns "less than 50 percent of Angioblast" and about 34 percent of Mesoblast. The Thorney-Thistle-Pratt group are substantial and have bought into all three capital raisings. The most recent substantial shareholder notices had Thorney and Thistle at 7.75 percent, a separate group Portfolio Partners and Aviva Group at 5.1 percent, with AMP reducing its earlier 11.55 percent holding to 6.9 percent on April 7, 2008.

The company has been as high as \$2.40 in January 2007, falling as low as 51 cents in April this year. It has recovered over the past two months.

Silviu has ensured control of the two companies while scrupulously absenting himself from board decisions that affect him. He has gathered together the intellectual property around stem cell development into tissue and the two companies reduce each other's costs.

"We saved ourselves \$20 million in scale-up and manufacturing and are getting twice as much for the investment dollar."

Angioblast can't undertake a capital raising without Mesoblast's permission and Donal O'Dwyer is Mesoblast's representative on the Angioblast board. The two companies have separate law firms and negotiations can be as hard as between any companies.

Silviu says there is a full range of options ahead. The two companies could be rolled together, Angioblast could be listed separately on Nasdaq.

"Today we don't know which way to go. It depends on how both the trials and the markets go."

Angioblast is investigating cardiac and other indications including eye disease, while Mesoblast focuses on long bone, spine and cartilage.

Silviu says the need is not for a systemic drug for knee cartilage repair, but for a local application.

"A single injection can protect existing tissue and probably make it grow."

It is at the end of the two-hour working lunch that we broach the question of board and management.

Silviu says he is driving a great team of executives and it is appropriate that the company has an executive director. Asked about the public and retail investor confusion about who is running the company he says nothing has changed in four years.

He says a corporate executive is not necessary if the founder can run the company. It is a formula a lot of institutional investors don't like, but Silviu refers to CSL's Dr Brian McNamee as a great example of a doctor successfully running a biotech.

"Running a business is not the definition of running a biotech," Silviu responds.  
"Management drives the company, the board provides oversight and governance.

"My interests are aligned with the people who have backed the company. I'm not going to make decisions based on being wedded to the company. If someone came out of the blue with the right offer, why wouldn't we consider it?"

Having brought Angioblast and Mesoblast to a series of US Food and Drug Administration approved phase I and II trials in a range of indications, Silviu sees no reason to step aside for a corporate chief executive officer, although he does say that his contract adviser position at Mesoblast is being discussed by the board and he is hoping that they will make the right offer.

Then he might change his title, but it would only be the title.

Mesoblast returned to the Biotech Daily Top 20 Index on July 1, 2008.

Mesoblast was up seven cents or 6.67 percent to \$1.12.