

THE QUÉBEC CONSORTIUM FOR DRUG DISCOVERY:

Facilitating Creative partnerships in Biopharmaceutical Research



Built as a first of its kind public-private partnership between universities, hospitals, biotechnology companies and the pharmaceutical industry, the Québec Consortium for Drug Discovery (CQDM) is doing its part as a successful collaboration model.

Established in 2008, the CQDM set out to put the needs of the pharmaceutical industry at the very centre of its concerns, while at the same time, it was looking for ways to allow both the public sector and the pharmaceutical industry to invest more into R&D and increase the productivity of its investments in Canada. To meet these criteria, the CQDM organized a competition where researchers from all milieus, whether it is industry or academia, would get the opportunity to take a unique project idea and create tools and technologies to accelerate the drug discovery process.

One year later, four outstanding projects are underway, all aligned with CQDM's mission, emphasizing the idea

of true collaboration, while at the same time satisfying a market niche, as well as the needs of major pharmaceutical companies and financial contributors to the project: Pfizer Canada, Astra Zeneca Canada and Merck Frost Canada.

"The projects were selected based on the impact they would have on biopharmaceutical research," explained Diane Gosselin, vice president, Research and Business Development CQDM. "What factored into our decision in choosing these four projects was the scientific excellence of these projects and their applicability."

"Overall we're happy to see that we gave clear directions in our call for proposals that was clearly satisfied by the projects that won out in the competition," adds CQDM president and CEO Max Fehlman. "In all the projects that were selected, there were both private and public components, the collaborations did not preexist but rather were built to fit our call for proposals."

According to both Fehlman and Gosselin, the added caveat is that the technologies that will be developed by the four winners of the competition are not to be commercialized but rather transferred and shared by the biopharmaceutical industry in Québec.

"For this reason, we chose projects with wide applications. In fact the wider the applications of the technology, the better," stated Fehlman.

One of the eventual winners of the competition that caught the attention of both Fehlman and Gosselin during the selection process was a project submitted by Caprion Proteomics Inc., seeking



Infiltration procedure. Photo: Medicago

to develop biomarkers for the measurement of early stage diabetes. The project, which is headed up by Eustache Paramithiotis of Caprion Proteomics involves unique cross scientific disciplines and includes co-investigators Marc Prentki, CHUM Research Centre, University of Montréal; and Remi Rabasa-Lhoret, Montréal Clinical Research Institute, University of Montréal.

"I would say that this is a perfect example of the type of project we were hoping to inspire, because firstly it's a collaboration that did not exist prior to the competition and secondly it is both industry and market driven in the sense that diabetes is a disease on the rise. I mean, the final component you have in this competition, is not the commercialization of the technology but rather the transfer of the technology to the industry," Gosselin said.

Paramithiotis says the decision to go after diabetes was strategic.

"The criteria used by the CQDM was pretty specific, they wanted industry and academic collaboration as a requirement and to enable drug development in a significant way, likewise Diabetes is a real problem socially and has some serious



"In all the projects that were selected, there were both private and public components, the collaborations did not preexist but rather were built to fit our call for proposals." — Diane Gosselin

challenges that have not quite been met in terms of figuring out the right types of treatment. It's also a disease that all three founding pharma's backing the CQDM have programs in," he said.

By developing biomarkers that accurately measure B-cell numbers and function, as well as biomarkers, Paramithiotis says that researchers will be able to predict patient response to specific classes of Type 2 diabetes treatments.

"The progressive loss of pancreatic B-cells or their function results in Type 1 and Type 2 diabetes. Both Type 1 and Type 2 diabetes are dependent on the proper functioning of the pancreatic islets. Moreover 90 per cent

of new diabetics are type 2 diabetics. Right now, we are lacking the ability to effectively measure the status of the pancreatic islets, how many are there overall, are they functioning properly. We aim to identify specific markers in the circulation of the pancreatic islet in terms of mass, number and functional state," he said.

Project researchers hope to accomplish this through the use of Caprion's proprietary CellCarta proteomics technologies.

"We think that with CellCarta, we can analyze secretory proteins of pancreatic beta-islet cells isolated from human and animal models of diabetes, as well as blood plasma collected from human

diabetes patient populations in order to discover and validate panels of protein biomarkers that are predictive of diabetes disease progression and of therapeutic response," he said, while adding that early stage markers will also help in pathogenesis, the therapeutic understanding of pathogenesis.

On what lead to the collaboration between the Montréal Diabetes Centre and the Clinical Research Institute of Montréal; both affiliated with the University of Montréal and getting researchers Mark Prentki, one of the most senior figures in Québec for diabetes research, and Remi Rabasa-Lhoret on board, Paramithiotis says he simply used the criteria of the CQDM application process as a means to best shape the project and come up with the most compelling proposal.

"I wrote Mark (Prentki) when the competition first came up, told him that we had a particular expertise in large scale discovery of biomarkers, and he had a particular expertise in diabetes, I asked him if we could combine our abilities. I knew I also needed a clinician to complete the triangle, and when I looked for clinicians involved in diabetes Remi Rabasa-Lhoret's name stuck out as well as his close proximity to our labs."

Having Rabasa Lhoret on board was key states Paramithiotis.

"Having the ability to work with the clinician fills a kind translational medicine component; it also provides input as to what the medical community needs from this discovery and from this technology."

The best part of all says Paramithiotis is that the three researchers were all right around the corner from each other. Not surprisingly, CQDM was impressed with this line of thinking.

"We were also fortunate that the three collaborating labs were recognized globally as authorities. Even more fortunate that we are all within three kilometers of each other and totally complimentary with what we can do. We are able to leverage our abilities to something greater than the some of our parts," he said.

This, says Paramithiotis, is where the true value of the CQDM lies.

"It created a mechanism, because they require an industrial academic interaction, and almost force the issue of trying to get together complementary skills sets. It also enabled us to actually go out and attract world class experts in a particular



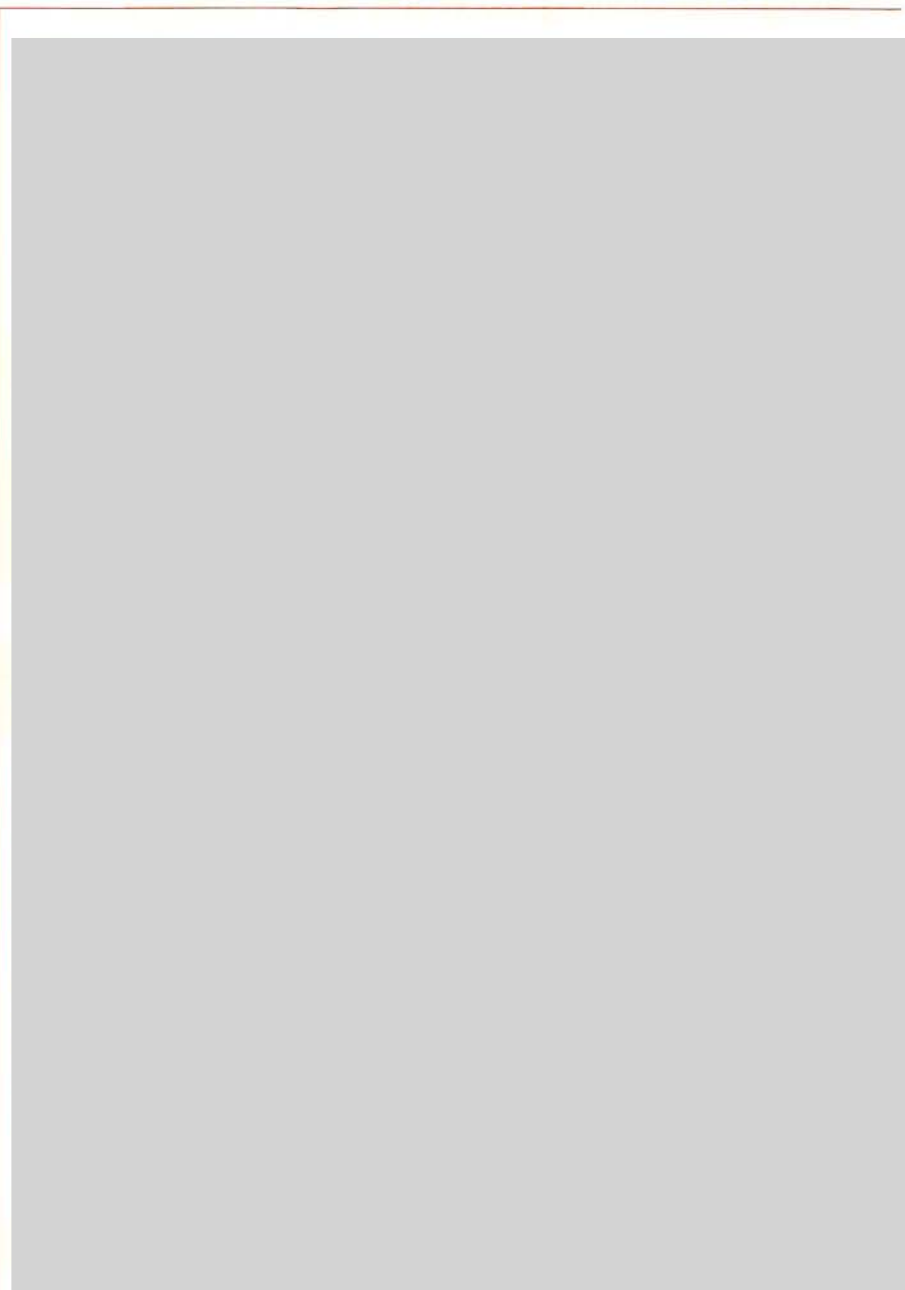
"For this reason, we chose projects with wide applications. In fact the wider the applications of the technology, the better." — Max Fehlman

field, get us to think about the way we do discovery and validation and think outside the box. I don't know if it was planned to work out this way in these tough times, but it has certainly helped

us to maintain jobs and keep our technical staff at the levels we had before."

It is something he says is unlike anywhere else in Canada.

"A lot of people over the years have





“Having the ability to work with the clinician fills a kind translational medicine component; it also provides input as to what the medical community needs from this discovery and from this technology.”

— Eustache Paramithiotis

spoken about getting universities and companies to collaborate with the big pharma's and it does happen with various degrees of success but not to this level I don't think. I may be a little biased as a winner of this competition, but even if I wasn't one of the winners, the thought of getting the private sector including both big-pharma and biotech together, as well as the public sector, academics and government into something tangible, well that is truly unique and special.”

While there's no guarantee that all the projects are going to work out that way, Paramithiotis feels that at least the CQDM has a framework, and he has no regrets about submitting his proposal

“What we're doing isn't basic discovery, at the same time it doesn't overlap with basic research that is mostly funded academically. Its also not clinical trial product development, but rather it's in that in-between area where we are facing the most difficulty. Americans call this area the valley of death, where you've got the initial discovery, but getting it to the point where you're actually running it in a trial, where all the development is you're faced with a lot of attrition. By the CQDM addressing them selves specifically to fill this need, it was very thoughtful on their part.”

Another winning project that both Fehlman and Gosselin felt particularly good about was Medicago's VLP express: a novel high throughput technology that has the potential to accelerate the discovery and development of new vaccine antigens based on virus-like particles (VLPs). The primary goals of this project are to accelerate the vaccine discovery process and to increase the efficacy of vaccine express. Louis Vézina, chief scientific officer Medicago Inc is the project lead, with co-investigators Alain Garnier of Laval University, Jean-Francois Harpin, SNC-Lavelin Pharma and Brian Ward on board.

“In terms of vaccine development, our project had many new and unique features and carried significant promises,” states Vézina.

“Vaccines are developed from antigenic regions of pathogen proteins. Identifying a strong antigenic component requires high-throughput production and testing. As most antigenic components are surface membrane-anchored proteins, production and presentation (presentation refers to how the antigens will be presented to the immune system) of these components has always been difficult, at any throughput scale. Testing multiple combinations of antigenic/presentation

components in animals adds to the development cost and time. Our proposed platform brings solutions to most if not all of these problems.”

Vézina adds that it stems from two robust technologies: an easily scalable and a cost efficient plant-based transient expression system, and an antigen presentation nano-particle developed from the influenza H5 virion. When it will be operating at HT scale, the platform is planned to handle hundreds of antigen combinations per week.

“These will be expressed as recombinant nano-particles (with the antigen presented at the surface of the particle as spikes) in a miniature plant-based biosynthesis device, extracted, purified and tested in vitro for antigenicity. As this is a miniature/automated replication of what Medicago does at far larger scale, transitioning from the miniature scale to the pilot and production scales will be seamless,” he said.

Vézina feels his project was chosen due to an increased interest in vaccine research and development, and the need for a fully operational discovery platform that can reduce time and cost associated with validating and screening candidate antigens. Likewise, how the technology functions as an enabling tool to drug discovery was also important. It is a general belief in the scientific community that vaccines can be developed that will trigger efficient protection against a far broader array of illnesses and conditions than those for which immunization is used currently. These include (but not only) some of the most significant global health threats such as malaria, dengue, HIV, HepC, pandemic influenza etc.

“This is going to be a tool for the new product development teams of vaccine companies. We expect the platform to be offered as a customized contract service at the beginning but it will subsequently be commercialized as a stand-alone development tool under license. It could also apply to the development of other biological molecules such as antibodies. Vaccine development is booming at the moment. There are hopes that efficient vaccines can and will be developed not only for pandemics but for several recurrent endemics and for chronic illnesses,” he said.

Like Paramithiotis, Vézina agrees that the project and the criteria set by CQDM encouraged him to work with scientists that he never thought he would work

with. Specifically, the Medicago project is being carried out by two private companies and two university-based research groups. It will combine Medicago's transient expression technology with expertise in process automation (SNC-Lavalin Pharma), VLP purification (Laval University) and pre-clinical evaluation.

"Bringing our current vaccine production platform to this miniature/automated format will require close collaboration between participants of various skills and expertises and extends well beyond our usual network. New teams involved in miniaturization, automation, small-scale high-throughput extraction and purification, in vitro testing are now essential to the successful development of the platform. So basically there are four groups: Our R&D team at Medicago, SNC-Lavalin for the engineering of miniaturization and automation, Alain Garnier from the University of Laval for the development of high-throughput and generic purification devices and Brian Ward of McGill University for the development of in vitro testing systems."

Overall, Vézina has nothing but praise for all the parties behind the creation of the CQDM, and appreciative of the active role big pharma has taken in this competition.

"It is a refined and very intelligent approach to funding that will have a tangible impact on drug development. It bears all the advantages of funding based on competition but has focused R&D goals, is based on deliverables and is tightly managed. The involvement of big pharma is also a significant incentive for biotech companies to get involved," states Vézina.

From both a biotech and also from the university perspective it's really a win-win situation knowing that if successful they will have pharmaceutical companies using their technology. Not surprisingly, as the CQDM prepares to pick the winners of this year's competition, excitement and interest competition is building according to Gosselin.

"Having a pharmaceutical company using and validating your technology, is really something that is really positive for the biotech companies such as Medicago and Caprion because, you know, they (this year's applicants) are looking for collaboration with the pharma industry. They are looking for



"In terms of vaccine development, our project had many new and unique features and carried significant promises."

— Louis Vézina

their technologies to be validated by the pharmaceutical industry."

Both Fehlman and Gosselin are also hopeful that the positive returns already realized from last year's competition will translate beneficially into this year's competition.

"I can tell you that we have a lot of interest for this year's competition," states Gosselin, while adding also that the CQDM has other big plans in store for the winners, including a new mentorship program where experts from the pharmaceutical industry will act as mentors for the winners

"For each winning project in this year's competition we will have three expert

mentors provided by our pharmaceutical industry partners who will be there to advise the principal investigators with their projects mainly on the applicability of the technology and how it can be oriented to have some real impact on biopharmaceutical research. This is something from a researcher's point of view that is seen as very positive," she said.

For this year's competition, companies have already submitted their letters of intent, with the announcement of selected letters to come on October 21, 2009, followed shortly by the deadline to submit full proposals on November 30, 2009.

The final selection announcement will be made February 15, 2010. ●

