Lab Report

Create Health's Borrebaeck on Using Chips for Clinical Research

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As of January 1, Swegene, a privately-funded non-profit microarray consortium, had run through its last budget and had to close up shop. But its director, Carl Borrebaeck, and his associates decided to use the five-year-old core facility as a springboard to a more integrated project with clinical research as the main objective.

Called Create Health (Clinical cancer REsearch using Emerging Advanced TEchnology for Health), the new cancer center was founded by experts in the fields of proteomics, genomics, antibody arrays, clinical oncology, nanobiotechnology and bioinformatics at Lund University in order to translate the technological advancements of the last half decade to the clinic, particularly in discovering biomarkers for cancer.

Funded through a state grant and located next to Lund University Hospital, the center will make clinical applicability of advanced technologies a primary focus and offer programs for masters and PhD students as well. To learn more about the new venture, *BioArray News* spoke with Borrebaeck, now Create Health's director, this week.

Why are you setting up this center?

It's a new initiative actually initiated by the Swedish Foundation for Strategic Research, to look at more long-term support of strategic research centers trying to create some novel [results]. And what we suggested to them a year ago was to set up a new cancer center, which is based on novel technology and novel technology development.

What we are doing is bringing together clinical oncologists, bioinformatics, proteomics, genomics people, and my background is immunology, to solve some very concrete questions such as why do some cancer patients live for one year and some others for 10 years with the same diagnosis — can we see any protein patterns that would help interpret this? In many cases, we start with the same therapy for cancer patients [and] some of them develop therapy resistance after a few years. Why is this so and can we predict that and individualize the treatment, based on disease associated protein signatures?

These are the questions that we'd like to answer based on this cutting-edge technology and its development. Some of that is based on different kinds of DNA arrays and a lot of it is based on antibody arrays for high-throughput proteomics that we've been working with for several years in individual groups.

This is the reason for the center. If you look at technology development, there are tremendously exciting technologies but then there is a gap of at least five years before it reaches the clinic, if it does at all. This is a large grant that will aim to bridge this gap and work with the clinicians directly and work with patients directly.

How much is the grant for?

We got $2 million a year secured and we are aiming for a number of other big grants as well, but the total budget is $5 million per year.

So tell me more about Center Health's team and how you will cooperate.

We are actually moving physically into a new center. It's a new house they are building for us; it's not one of those virtual centers, organizational centers that are all around the world. We are actually moving in together — nanotechnologists, oncologists, immunologists, bioinformatics people.

[As for the team], we have got Åke Borg [professor of Experimental Oncology at Lund]. He's the genomics guy and involved in clinical oncology, working a lot with breast cancer with the same type of questions, but with DNA arrays like expression arrays, tiling arrays BAC arrays, and so on. Peter James is [well-known] in proteomics and a well-known mass-spectrometry user. Thomas Laurell is well-known in nanotechnology, he's developing the miniaturization of arrays and different interfaces between the arrays and mass spec.

Then we have Carsten Rose [the director for the Department of Oncology at Lund University Hospital]. He is head of the oncology department — he probably has more than 300 physicians working for him, but what's more interesting is that he' s just set up a clinical research unit where we can have access to all the patients and all the patients' material. So he would be a provider of that through his expertise.

We are also working with Sven Påhlman who is a tumor biologist. He works on various aspects of the tumor information like hypoxia and how that affects the protein signatures and so on. Finally, we are working with Carsten Peterson [head of Computational Biology and Biological Physics at Lund], who is really one of the well-known bioinformaticists. He has developed programs used in more than 50 different countries, like BASE, for microarray analysis. He will of course take part in the biobank building we will do and in all the analysis of the protein arrays, antibody arrays, and so on.

That leaves yourself, the director. How are you qualified for this position?

I have been working with B cells and B-cell tumors for the last 10 years. I have been working with antibody engineering for 20 years. We set up DNA microarrays in 1999 and we since then developed our own antibody microarray platform which is very competitive. We've engineered recombinant antibodies directly applicable for microarray applications. That has resulted in projects where we are now running clinical tests with an antibody microarray platform. I have also previously been heading large scientific projects.

So I am coming from both sides, both the DNA microarrays for genomics and antibody arrays for proteomics and also with the lymphoma B-cell tumor part. We are going to focus on B-cell tumors and breast cancer. Those are the two cancers that [we] will initially look at at least.

How does this carry over from Swegene in terms of your objectives and the technology you are using?

Swegene was basically set up with two wings. One was we got a lot of money for so-called 'resource centers' where we set up a core facility where we ran proteomics and DNA microarrays as a service to all scientific and commercial scientists that were interested in getting a high-quality microarray.

The other arm of Swegene was developmental programs where we also received money for several years focusing on antibody microarrays.

Swegene is no more. It [was funded through] 2005-2006. So what we are doing now is taking the best part of Swegene and using that for a sort of direct and focused activity on cancer based on the technologies that we developed. It's not that we are starting from scratch at all. We've been doing this for five years, and we have very experienced people so they've been doing this for a long time.

Most of Swegene's staff will go into the new center, which we call Create Health, and set up a bigger genomic center where we will develop all kinds of new arrays.

Now that you have this opportunity to build a brand new place, are there any new tools that you are interested in integrating into your work?

Antibody microarrays have been talked about for a while, but there are still really few good applications. If you search for antibody microarrays on PubMed you get 15 hits related to cancer. I still think it has a tremendous opportunity but one of the major challenges [we are facing] is that people haven't really been aware of challenges of this technology. If you are good at mass spec, if you are good at surfaces, if you are good at proteome labeling, it's really not enough. You have to have an integrated approach where you start with the molecules and engineer them to be the best, collaborate with nano people that can do anything with surfaces and so forth. That is one of the major challenges we face — to integrate all of this, not only into a platform you can publish a paper on, but really is robust and can be applied for cancer patients. This in combination with high-throughput mass spectroscopy is also of the highest interest.

In combination of course, we will look at very minute proteome preparations from laser capture microdissection, for example. We are also looking at nano arrays where you can have tens of thousands of data points on the surface, and to do that you have to miniaturize the whole thing. These are research projects that go side by side with the more clinical research projects, but it demonstrates that we are not stopping development now when we go into the clinic, but we will actually do it hand in hand. We will directly apply it to patent samples.

Also, in Scandinavia, and Northern Europe, there's nothing [else] like this. They talk about [integrating clinicians with technology development people] a lot, but it's mostly talk. There are very few examples of a completely integrated center like this [in the world].

So why is this happening at Lund?

Well I think it's grant money really. It costs a lot of money to integrate these people, and just to have the antibody microarrays is costly and to do it completely with nanotechnology people and bioinformatics — it costs a lot of money.

But it's happened here because we have all the experts and the resources. We have access to the biobanks, which is unique for Sweden, we have a register that you can follow cancer patients years and years back where you have all the journals and all the information. Which is good because you can do partly retrospective studies. So it's a combination of all the points.

We've been able to do all of this because we are an academic site and we can spend all the money we can apply for and we don't have to think about selling it. The real value in this is not of course in the platform, but what we discover in the clinic, on biomarkers. My own interest is primarily in antibody-based therapy, and if we can find new markers for that that would be very interesting.

Why have you chosen to focus on breast cancer and lymphoma?

Breast cancer is one of the biggest cancers in the world and lymphoma is one of the most rapidly growing cancers and one that is very difficult to get a proper diagnosis. Those are the clinical reasons.

Another reason is that we have been working on this for many years, so they are sort of our 'favorite' cancers. So initially we will focus on these, at least for the first two or three years.

So when will you be going live with the center?

We will physically be moving in the second week of May. That's the official celebration where we have the champagne. We have already started working as a team, but officially we will be moving in in May.

We will be located at Lund's Biomedical Center, which is a new building, and there will be between 60 and 70 people working there.