Interview

Thi-Sau Migone speaks to James Eslea-MacDonald on the upcoming *World ADC San Francisco 2013 conference*, 14th – 17th October 2013, San Francisco, CA

Dr. Thi-Sau Migone
Chief Scientific Officer
Igenica

Dr. Thi-Sau Migone joined Igenica in 2013 as Chief Scientific Officer. She has wide-ranging experience in discovery and development of novel therapeutic antibodies in the fields of autoimmunity, infectious diseases and oncology. Prior to Igenica, she was at Human Genome Sciences, where she held a variety of executive positions and most recently served as Vice President of Research. In that role, she led scientific programs ranging from early discovery through Biologics License Applications, including belimumab and raxibacumab, two antibody programs that reached regulatory approval under her scientific leadership. Prior to Human Genome Sciences, Dr. Migone held research positions at DNAX Research Institute, the National Heart, Lung and Blood Institute and National Institute of Allergy and Infectious Diseases.

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Firstly congratulations on joining Igenica; how have the first few months been for you?

It's been a very interesting few months; I had been at Human Genome Sciences for over twelve years and so was very established in a larger public company with collaborations with big pharma. However I was looking for something where I could continue to have a real impact on the scientific strategy and a start-up like Igenica certainly fits this bill.

What we have under one roof is a mini-biotech and I feel it has great potential. There is a lot of work to do but the programs are very interesting and challenging, so I'm happy with my decision. We have a bright future in front of us and I believe we can make a difference in the field because of the types of targets and the platform technologies that we can combine to generate new therapeutics.

What does it feel like working in the ADC field at the moment?

I am so happy to be working in this field now. I started working in ADCs approximately three years ago but it wasn't the complete focus of my work and I felt it was still an area that was in development. Now, with a couple of products approved, there is a clear regulatory pathway for us to follow. There are a lot of different technologies that are being developed at the same time and there is clearly a lot of interest.

It is a chance to leverage targets that without cytotoxic agents would probably not have become therapeutic targets in cancer. So we can go after really interesting and novel proteins. At the same time I think that the ADC field is just becoming much more competitive, so it is important to work rigorously, quickly, and make the most of every opportunity one has to do good experiments, be able to talk about and to find good partners. It's a very exciting field at this time.

What's the most exciting project that you're currently working on?

We have several really interesting projects that I'm looking forward to working on. One is a completely novel target that we've found, which is expressed in low copy numbers. However its expression is restricted and it lends itself to be developed as an ADC in the hematologic field. Another target is something that is expressed at a higher copy number, but again is restricted in colon cancer. I'm excited that we have projects that are new targets that allow us to have pre-clinical programs in different therapeutic areas. We plan to develop these further with our own proprietary ADC technology and take these forward into the clinic.

You alluded to this and I'm keen to ask, there's a lot of talk about what the ingredients of the perfect ADC target are, what's your view?

Clearly when I think about ADCs, you have to have all of the right ingredients together if you want to make something that is going to be really successful. It starts with the target, you have to have a target that is restricted enough in it's expression and you obviously do not want it in vital organs. You also need a highly specific antibody that internalizes and is cross-reactive with the cyno target to allow toxicology evaluation. Then comes the linker, you need to think about whether you want site-specific conjugations and cleavable versus non-cleavable linkers. Then finally the cytotoxin payload itself, and depending on the type of tumor that you're going after, different cytotoxic mechanisms will come into play.

"Understanding where you're conjugating your drug to is becoming much more important"

I think as we work in the field more, understanding where you're conjugating your drug to is becoming much more important and that is evidenced by the fact that there are more platforms that are trying to provide site specific conjugation. This was something that wasn't really important 4 or 5 years ago but now there are a number of companies that are working very hard on that. Knowing where the drug is attached and how much of the drug you have on, your drug-antibody ratio, is important. It allows you to have more consistent results, predict what you can do from a manufacturing perspective and also from a PK and safety perspective; it gives you a reassurance of what you're going to see. I think this is where the field is moving to and you can see that from the big players, like Seattle Genetics and Genentech, who are moving towards a more site-directed approach than they've used previously.

Site-specific technology definitely seems to be at the fore-front for many ADC developers at the moment. One of the other hot trends within the antibody field at the moment is multi-specificity, do you think that this is a route that ADCs could take as well?

I think they could, it makes sense based on what a bispecific antibody can lend. Initially we had thought of bispecific antibodies as a way of bringing in accessory cells to the target, such as T cells, therefore allowing a more efficient effector response. But I think what we can do now is make the recognition of the target more specific by using these different multi-specific approaches.

It's going to be interesting to see whether you can still have good internalization along with enhanced specificity, whilst maintaining the relative affinity of

the two arms. This is something that will require a lot of work and its success may depend very much on the actual pairing. This is something that will undoubtedly be explored.

Looking at Igenica now, you've managed to secure a lot of funding since your foundation, what's been the secret to your success?

We are lucky in having very committed Venture Capitalists who saw the potential in our platforms. When Igenica was founded it was really based more on the ability to find new tumor specific antigens using our mass-spec proteomics approach and then having our proprietary antibody platform.

On top of that, now that we've added our proprietary ADCs, the same group sees the potential to really make a difference in the field. This brings together these three cornerstones within Igenica. We've also demonstrated that we can move things forward. We've just filed our first IND two weeks ago, which for a small company like us is a big milestone, that shows we can deal with early discovery as well as rigorous pre-clinical development and now we're ready to put our first program into the clinic.

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What then do the next twelve months hold for Igenica?

We have the challenge of our first clinical stage program and that requires a completely different type of interactions with CROs and KOLs. We're very lucky to have a very experienced clinical lead, in Dr Bill Ho who came from Genentech and who ran a lot of early IND programs there.

That's going to be one area of focus and the other area is the ADCs. As I mentioned, we have a number of targets that are in the validation stage that we want to take into IND enabling work.

We're also looking forward to partnering our technology. Because of it's flexibility I think that it lends itself to be used by companies who may have antibodies or targets but may not have the right toxin or are not achieving homogeneous conjugation. This is what we can provide, in that we can, not only achieve homogeneous conjugation but we also have a proprietary toxin. We can bring a lot to a potential partner and we are working very hard on that as well.

You're involved in our World ADC Summit in San Francisco next month, what personally are you looking forward to?

I'm really excited that it is right here in our backyard and I'm looking forward to hearing first hand from all of the different companies that are involved in the area. Both from a technical and scientific perspective, what they're focused on and what their main interests are.

I'm looking forward to a lot of networking. There are a lot people who are moving into this space that I've known from my previous life where we did more traditional antibody drug development and they're now really focusing on ADCs. I'm looking forward to catching up with them and telling them about what we do.

I didn't attend last year, but some of my colleagues did and they thought it was a phenomenal meeting. We've already arranged a

number of meetings for people who are coming from Europe and who are attending and we will be able to catch up and give them an update on where our technology is. We're very excited and we have a large contingent from our small company attending, both from the chemistry, biology and business development sides.

Igenica will be presenting at the World ADC San Francisco 2013 conference taking place in San Francisco, CA, 14th – 17th October 2013.