Cancer vaccines: looking to the future

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Interview by Jenaid Rees (Commissioning Editor)

Vasso Apostolopoulos has been working in the field of cancer vaccines since 1991, and human clinical trials on her work have been conducted since 1994. Her work has been at the forefront of scientific research into the development of a vaccine for cancer and she has received over 90 awards and honours in recognition of her achievements. Some notable awards include, the Premier's Award for medical research, was named Young Australian of the Year (Victoria), recipient of the Channel 10/Herald Sun Young Achiever of the Year Award as well as being awarded the Order of Brigadier General of the Phoenix Battalion by the Greek President. In 1998 Apostolopoulos received the NHMRC CJ Martin Research Fellowship and worked at the Scripps Research Institute in California, USA, for 3.5 years and returned to the Austin Research Institute (VIC, Australia), and headed the Immunology and Vaccine Laboratory receiving the NHMRC RD Wright Fellowship. Upon her return to Australia, Apostolopoulos received the Victorian Tall Poppy Award, the Bodossaki Foundation Academic Prize, was inducted into the Victorian Honour roll of Women, was a torchbearer for the Melbourne leg of the International Athens 2004 Olympic Torch Relay, was named Woman of the Year, and is an Australia Day Ambassador. Her contribution into cancer research, vaccines and immunology has been extensive – publishing over 200 scientific papers and books, an inventor on 14 patents and collaborates with over 50 national and international Research Institutes and Universities. Her current research interests are in the development of new improved cancer vaccines and new modes of antigen delivery for immune stimulation. She is also interested in chronic diseases treatment and prevention through immunotherapy. She serves on the Editorial Board for *Expert Review of Vaccines*.

What inspired you to specialize in the field of cancer vaccines?

Cancer affects everybody in some way and I wanted to add my little piece to the puzzle. I wanted to do cancer research, so I undertook an honors project on developing monoclonal antibodies to a protein, mucin 1 (MUC1), highly expressed on cancer cells. This was very successful and led into a productive PhD project. Half was through my PhD, I was approached by my supervisor, and great mentor, Ian McKenzie (Austin Research Institute, VIC, Australia) to start a new unknown project, into developing a vaccine for MUC1 expressing cancers. The risks were high, that I would not yield any results, as I was already productive in my initial project. I took the chance, changed projects, and the rest is history.

You were involved in the development of the worlds' first vaccine for breast and ovarian cancer; what do you feel is the impact of this work, both therapeutically and on the field of cancer vaccine development?

Today every second research laboratory is developing an immunotherapeutic approach (vaccine) for cancer. Numerous immune cell activation receptors and ligands have been identified, and, methods of antigen delivery are exponentially increasing. Over 20 years ago, when I began in the field of vaccines, not much was known on how to stimulate the immune system. Dendritic cells were quite new, TLR receptors were unknown, cell surface receptors for antigen targeting were limited. The approach that was used, together with my colleagues, Ian McKenzie and Geoff Pietersz from the Austin Research Institute (VIC Australia) at the time, was to target the MUC1 antigen to dendritic cells in order to stimulate T cells. Mannan (a poly-mannose) was conjugated in a unique method to MUC1 protein, and this was used to

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target the mannose receptor on dendritic cells. Now it is known that mannose also binds to DEC205, DC-SIGN etc receptors, though these receptors were unknown at the time. This resulted in strong immune specific stimulation and eradication of tumors in mice. These results led to studies in rats, chickens, rhesus macaque monkeys and quickly into human clinical trials in patients with cancer. These studies paved the way to antigen targeting approach for vaccines and mechanisms of immune stimulation. With the plethora of information that are available today, using antigen targeting approach to receptors on APC, such as, dendritic cells, new, improved cancer vaccines will result.

■ Much of your work focuses on tumor-associated MUC1 glycoprotein and cancer vaccines; what is the current status of this research?

The vaccine is being developed for commercialization by a pharmaceutical company. They are currently focusing the development as an ovarian cancer vaccine, however, other MUC1 expressing cancers will also soon follow in their development.

■ You have been working in the field of cancer vaccines for over 20 years; what research do you have on the horizon that you feel is particularly promising?

The other part of my research involves the use of mannan to develop a vaccine against multiple sclerosis (MS). Together with my colleagues at the University of Patras (Greece), John Matsoukas *et al.*, the use of mannan conjugated in a unique mode to peptides from MS antigens, diverts immune responses and inhibits MS symptoms in animal models. These findings are very promising and Phase I/II clinical trials in humans with MS will begin within 1–2 years.

■ You have been heralded as an inspirational woman in the field of vaccine research; how do you feel about this and what has been the biggest influence on your career to date?

It is satisfying to see all the hard work and endless hours in the lab being recognized nationally and internationally. The most satisfying is seeing the positive data from patients being injected with the vaccine. My biggest influences have been my father and Ian McKenzie. Both in their own ways, have taught me to try anything, do anything, get in there and do it, and that even a failed result leads to a successful outcome.

■ Of your scientific achievements, which one do you feel will have the biggest impact on the field of vaccines?

Antigen receptor targeting approach to dendritic cells for T-cell stimulation.

■ In your eyes, where do you feel the field of cancer vaccines will be in the next 5 years?

People think that technology is moving at a fast pace, in other words, 5 years ago there were no smart phones, no smart tablets, no digital and smart TVs, no social media of which we all rely on today. If we go back 15 years ago, there were no digital cameras, no flat screen TVs, no internet, mobile phones were not popular, email accounts were limited. At the same rate, medical research is also moving along. In the next 5 years, new improved cancer vaccines will be developed with an exponential output of data from human clinical trial testing. If we think the next 15 years…? many cancers will be treatable and life will be prolonged in cancer patients.

■ Do you have any words of advice you would give a young researcher entering the field of cancer vaccines?

Never give up and keep going. Remember, Thomas Edison was once asked after his 5,000th failed experiment, "you have failed 5,000-times, just forget about it, you will never discover light", his reply was, "ahh I've discovered 5,000 ways of how not to make light…"

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