Interview

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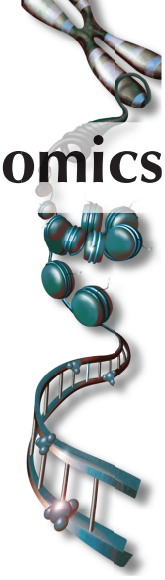
Epigenomics



Neuroendocrine prostate cancer: long noncoding RNAs to treat an incurable cancer – an interview with Dr Francesco Crea

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Francesco Crea speaks to Lucy Chard, Commissioning Editor. Dr Crea's lab studies the role of epigenetic factors and noncoding RNA in cancer initiation and progression. While working at the National Cancer Institute (USA), Dr Crea has demonstrated that polycomb-targeting drugs eradicate prostate cancer stem cells. While working at the BC Cancer Agency (Canada), Dr Crea discovered and patented *PCAT18*, a long noncoding RNA involved in prostate cancer metastasis. Dr Crea has received awards from the American Society of Clinical Oncology, from the Prostate Cancer Program and from Prostate Cancer Foundation BC. He is also an Editorial Board member for *Epigenomics*. His team is currently working on developing new biomarkers and therapeutic targets for incurable prostate and breast cancers.

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Could you please begin by introducing yourself, your background & your work to date?

Francesco Crea, I am a senior lecturer in cancer genetics at the Open University and my background is in cancer therapeutics, particularly related to prostate cancer (PCa).

Please describe the work you are currently conducting on 'Clinical characterization of treatment-emergent NEPC' which you have given a talk on this morning at NEPC 2019?

Our group is interested in a particular subtype of PCa which is called neuroendocrine prostate cancer (NEPC). This subtype was thought to be very rare but with the emergence of new types of therapies, particularly abiraterone (Zytiga) and enzalutamide (Xtandi), there are studies showing that this disease, which is a very aggressive disease, is much more common that we first thought. We are working to try to identify new biomarkers and new therapeutic targets for this unrecognized type of cancer.

What are the implications of this work on the epigenomic field & in the clinic?

From an epigenetic point of view it is a particularly interesting model for us to study because there are no genetic alterations which drive this progression to neuroendocrine PCa. Therefore, we think that epigenetic modifications, particularly histone modifications and lncRNAs, are the drivers and we and other groups are investigating the role of specific epigenetic alterations and lncRNAs in this process.

What do you see as the biggest area of growth for cancer therapy research in the epigenomic field?

The most immediate area is the development of new epigenetic therapies. There are a few therapies which are already in the clinic or very close to being used in the clinical setting; so, if we are able to identify the critical epigenetic factors in NEPC, we already have the tools to inhibit them. Once we can combine these with a personalized approach to identifying, for example, with blood markers or urine markers, which patients are more likely to respond to certain types of epigenetic therapies, this could have a transformative impact on the therapy of this cancer which is thus far incurable.

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You are working with charities on this project, can you go into more detail on the involvement & role they play?

Our work is mostly supported by Cancer Research UK (CRUK) by the drug discovery program and by the early detection program as well. We have been working with them in many different ways. We are also involved with the local PCa support group and have been raising awareness about PCa – in particular about this new type of PCa. It is a particularly important interaction for us to have because the charities give us the perspective and urgency from the patients, so it helps to direct our research towards real life, meaning it is not just theoretical but rather is based on that specific pathway and using that pathway to change lives.

Do the charities come to you with a specific goal in mind?

In the case of CRUK, they have strategic goals that are achieved by specific grant calls to which you can apply. In the case of more local charities, they are interested in anything which can improve the survival or quality of life of PCa patients. Through the charities we collaborate with local clinicians, like Henry Andrews, of Milton Keynes University Hospital, interacting to find the best ways of bringing therapeutics into the clinic.

Therefore you will be better able to make the research more translatable?

By going to these types of meetings, with patients and families, they help you to understand what the critical need for certain types of patients and there are a few instances where we changed the direction of our research based on the conversations with patients. They are critical for our research in these early stages.

What do you hope to achieve in your career? What are your long-term scientific goals?

The long term goal of the lab is to identify new therapies and new biomarkers for aggressive and incurable cancers. Our main focus is neuroendocrine PCa and we have other projects which are also ongoing about brain metastasis from breast cancers and some primary pediatric brain cancers. The common theme is that we try to identify new epigenetic or long noncoding RNA-based therapies because we think that these are critical for prediction and patient outcomes and are relatively understudied – there is much more to it than has been found so far.

Financial & competing interests disclosure

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