

MOLECULAR CUISINE

Chris Griffiths

Psoriasis: a personal peripatetic path of discovery

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Discovery pathways from research leaders in the ESDR KITCHEN

Q & A

The following questions raised during the above session were answered by Chris Griffiths. For further information, he can be contacted at Christopher.Griffiths@manchester.ac.uk

Q: Bernhard Homey

Could you hypothesize, or if you have evidence, why is psoriasis so important for the human being that it is conserved all over the world in a relatively high prevalence, and in a similar prevalence in the different areas.

A: The prevalent theory as to the high prevalence of psoriasis, particularly in Northern Europe, is that in the pre-antibiotic era carrying the gene(s) for psoriasis may have been protective of dying from overwhelming strep infection. Thus, survival came at the expense of developing psoriasis but perhaps being a strep carrier.

Q: Bernhard Homey

If we know that the Th17 and IL-23 pathway is important and knowing that yeast infection is controlled by this, from our current perspective yeast infection is not a major problem but somehow psoriatic inflammation is an exaggeration of this archetypic immunological response. Do you think for early human beings this kind of immune system was important?

A: The short answer is yes I do think this was important as fungal disease is a significant issue still in least developed parts of the world.

Q: Elizaveta Gribaleva

Can I please ask if there are any potential biomarkers which could predict the response of patients to biologics?

A: A good question and one that we in the UK are working on in an MRC funded academic-industrial consortium on stratified medicine known as PSORT (Psoriasis Stratification to Optimise Relevant Therapy). Psoriasis is a complex disease and response to therapy will not be a consequence of a single biomarker but systems approach of clinical, genetic and immune biomarkers. The consortium has identified that HLA-CW6 conveys a greater chance of a PASI90 response to ustekinumab; also having palmar plantar psoriasis is marker for a poorer outcome to any biologic. These are but two of several examples but my guess is that stratification to drug response endotype will be a multi-omic algorithm.

Q: Nikolas Haass

Are there other species that develop psoriasis naturally?

A: No

Q: Lynda Grine

It seems that psoriasis is on the right path to have a good and solid treatment/disease management approach. To what other diseases can we translate our knowledge, and are your programs/institutions doing this? What advice do you have in this context?

A: Psoriasis and the translational research process that has been applied to it over the past 20-30 years is an excellent template for other chronic inflammatory skin diseases such as atopic dermatitis and alopecia areata

Q: Mari Løset

What are your thoughts on using preventive therapies (e.g., statins) among patients with moderate/severe psoriasis to reduce cardiovascular risk?

A: I think this is an excellent idea but requires a controlled study to ascertain benefit or at least a study to ascertain whether all patients with psoriasis would benefit from statins or just a subset. There are some data that appear to show statins per se being anti-inflammatory.

Q: Kiarash Khosrotehrani

If you push your reasoning, could we predict in the general population those at high risk of developing psoriasis and if so would immune intervention would reduce the onset of disease?

A: Yes and early intervention perhaps with an anti-IL23p19 may be beneficial in this regard.

Q: Roopesh Singh

Can we predict the Psoriasis associated co-morbidities in the patients based on their response to treatment response? I mean is there a trend in the occurrence of certain Ps comorbidities in the patients -demographics or any other factor?

A: Stratified medicine using systems medicine approaches rather than single biomarkers will I hope allow us to predict which patients are at higher risk of arthritis, cardiovascular diseases etc. thus enabling a preventative approach.

Q: Marion Bonnet

A lot could be learned from early events in psoriasis development. How can we reach out to communities in order to raise awareness on psoriasis and have access to patients at very early stages of the disease?

A: I agree. This is the reason we set up the rapid access clinic in Manchester. The earlier we see patients in the disease cycle the greater the chance of preventing comorbidities and progression to severe disease and perhaps with early intervention with biologics modifying the disease. The immune profile of these patients will be quite different that what we usually see.

Q: Daniel Kaufman

If psoriasis is a systemic disease, why is it most often limited to specific areas of the skin?

A: The disease itself is a skin disease but it has a number of associated medical conditions that are also inflammatory. Why plaques are so well circumscribed is still one of the mysteries of psoriasis but all of

the skin is capable of being involved and indeed Langerhans cell studies (which I didn't have the time to discuss) show that the clinically normal skin is in fact abnormal.

Q: Maria Laura Galimberti

Do you think the peripheral nervous System interacts with inflammation in the pathophysiology of disease? Could this be an escape system for non responders?

A: Yes it does. Peripheral nerves are required for the inflammation to be present. I am not sure I understand the second part of your question. Sorry.

Q: Becky Klein

Is there a concern with long term safety of immunosuppressants if the treatment paradigm is switched to a proactive approach rather than a reactive approach?

A: In short yes. That is why the registries are so important but so far the biologics as a class appear to be remarkably safe.

Q: Nicole Ward

Can you comment about how you execute your vision - which is so clear and incredible....how do you recruit the right people? How do you mentor them? How do you achieve such a staggering success with so many people? (This is a good question for investigators who are just starting their own labs...and for us old folks...who are amazed at how he does all of this)....

A: Remain curious and recruit people who are equally curious, questioning and better than oneself.