

PRESS RELEASE FROM FUTURE SCIENCE GROUP

March 2010

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Oral immunotherapy effective in fighting TB

Tuberculosis is a prevalent and damaging infectious disease – approximately one third of the world's population is infected. Of those people with latent infection, approximately 10% will develop clinical disease at some time during their lifetime.

Immunotherapy can be used to revert the disease-associated immune response of affected patients to that of healthy people. The most promising of such approaches has been to use heat-killed suspensions of the *Mycobacterium vaccae* combined with chemotherapy. Repeated doses of *M. vaccae* are safe and very effective, but a major problem is to move from an injectable form to an oral form in order to prevent the multiple use of syringes in areas with a high incidence of HIV and tuberculosis infection.

Now a team of collaborating scientists from Argentina and the United Kingdom have reported their experience in the use of oral *M. vaccae* in man, comparing the results obtained with those from a recent small study using three injected doses. They provide the first account of successful use of an oral immune modulator based on a preparation of a heat-killed Actinomycetales species in man, and the first potential major contribution to Directly Observed Therapy Short-course (DOTS) – used world-wide for the treatment of tuberculosis – since the development of pyrazinamide. The results are published in the March issue of *Immunotherapy**.

The patients in both the triple injection study and the study of oral administration came from the same local population, were of the same age ranges, and attended the same hospital in Rosario, Argentina. The results of clinical, bacteriological, radiological and immunological tests paralleled those achieved with earlier studies of injected *M. vaccae*. The only exception was in levels of TNF- α produced by cultured monocytes, where oral treatment failed to cause the reduction with time observed in those treated with injections.

Material was only available for ten patients with pulmonary disease caused by fully drug susceptible tuberculosis, all of whom were HIV seronegative and diagnosed with tuberculosis for the first time. Practical considerations and reagent availability prevented the conduct of a conventional, randomized, blinded, placebo-controlled trial. Nevertheless, the results strongly suggest that immunotherapy with heat-killed *M. vaccae* is as successful when administered by the oral route as it is by intradermal injection. Both injected and oral *M. vaccae* achieved significantly better results than did DOTS chemotherapy on its own. Oral *M. vaccae* should be very effective against drug-resistant strains, as previously shown with the injectable formulation.

Team leader Dr John Stanford of the Centre for Infectious Disease & International Health, University College London, said, "Now that immunotherapy with oral *M. vaccae* in frequent doses has been successfully demonstrated in tuberculosis, albeit in our very small study, its use in a whole range of important diseases can go forward. Needed now are phase II and III regulatory trials to satisfy the requirements of the MHRA and pharmaceutical control bodies in Europe and America."

The efficacy of the oral formulation should make the introduction of *M. vaccae* into the DOTS program of treatment, and indeed into the treatment of the many other diseases that respond to this immunotherapy, simpler than was the case with the injectable form.

Dr Stanford believes that the *Immunotherapy* paper is probably the most practically significant contribution that he and his collaborators have made towards achieving acceptance for the potential of effective immunotherapy by bacterial immune modulators. He says, "What we now badly need is support to prepare a GMP product to enable us to carry out a phase II, randomized, double-blinded, placebo-controlled, trial to the standard of Good Clinical Practice (GCP), in pulmonary tuberculosis. Given significant positive results from such a study, we could take forward a whole range of bacterial immune modulators into major developed and developing world diseases".

*Dlugovitzk D, Notario R, Martinel-Lamas D, Fiorenza G, Farroni M, Bogue C, Stanford C and Stanford J. Immunotherapy with oral, heat-killed, *Mycobacterium vaccae* in patients with moderate to advanced pulmonary tuberculosis. *Immunotherapy* (2010) 2(2) 159-169.

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NOTES FOR EDITORS

ABOUT IMMUNOTHERAPY – *Impact factor 6.09 (2008)*

Published bi-monthly; ISSN 1750-743X – Volume 2 (2010)

Citations: EMBASE/Excerpta Medica, Chemical Abstracts

The field of immunotherapy is moving forward at an unprecedented rate, and a range of therapeutic approaches are now used in clinical practice, often with outstanding success. The valuable role of immunotherapy in oncology is increasingly recognized alongside conventional chemo- and radio-therapies, and the US Food and Drug Administration has approved the use of immunotherapy in melanoma, leukemias, lymphomas and myelomas, and in breast, cervical, ovarian, kidney, prostate and colorectal cancers. Immunotherapeutics are also being applied in a variety of other disease areas, including allergy, rheumatoid disease, autoimmunity and transplantation, as well as in many infections, such as HIV/AIDS and hepatitis.

Many aspects of the immune system and mechanisms of immune-modulated therapies remain to be elucidated in order to exploit fully the emerging opportunities. Those involved in the research and clinical applications of immunotherapy are challenged by the huge and intricate volumes of knowledge arising from this fast-evolving field. Immunotherapy offers the scientific community an interdisciplinary forum, providing them with concise and most recent advances of various aspects of immunotherapeutics to aid navigation of this complex field.

Articles published in *Immunotherapy* include key areas such as:

- Cancer immunotherapy, including cancer vaccines and passive immunotherapeutic approaches
- Combined chemo/radioimmunotherapy in cancer treatment
- Restorative immunotherapy for AIDS and other immunocompromised patients
- Suppressive immunotherapy for autoimmunity diseases and transplantation
- Allergy vaccines
- Basic science of immunotherapeutic approaches
- Drug-immune system interactions

- Drug delivery systems, drug combinations and drug–drug interactions
- Summaries evaluating newly approved immunotherapeutic agents
- Newly identified immune targets of drugs
- Results of recent findings and clinical trials relevant to the field of immunotherapy
- Postmarketing research, including adverse events, drug safety, pharmacoeconomics and cost–benefit issues
- Immunotherapy delivers essential information in concise, at-a-glance article formats. Key advances in the field are reported and analyzed by international experts, providing an authoritative but accessible forum for this vitally important area of research.

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