

**Dr Mohammed Alsharifi**

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<b>Research</b>	Virology and Immunology

Mohammed grew up in Babylon/Iraq and studied Veterinary Medicine at Baghdad University. He was increasingly interested in medical research and after coming to Australia he studied Biomedical Science at Monash University. He then moved to the Australian National University to take up a PhD scholarship at The John Curtin School of Medical Research, and investigated with Arno Müllbacher, Robert Blanden, and Mario Lobigs the immunobiology of an alphavirus infection. During his early years in research he discovered a period of exhaustion in type-I interferon response following an acute viral infection, which may explain the clinically known observation that virus-infected patients are at increased risk to a more severe secondary viral and/or bacterial infection. Following the completion of his PhD studies, he investigated with Prof Müllbacher the possibility of using gamma-irradiated influenza virus as a universal flu vaccine. In 2008, he was awarded the Hanson Fellowship to continue his research into the universal Flu vaccine and also to investigate the possibility of producing other viral vaccines using similar technique to that used for influenza. His flu vaccine research has been featured in the Catalyst program on ABC (<http://www.abc.net.au/catalyst/stories/2613604.htm>), and in many newspaper articles such as (<http://www.news.com.au/adelaidenow/story/0,,25625291-5018662,00.html>) and (<http://www.news.com.au/adelaidenow/story/0,22606,25406694-5006301,00.html>).

**Selected publications:**

Alsharifi M, Furuya Y, Bowden TR, Lobigs M, Koskinen A, Regner M, Trinidad L, Boyle DB, Müllbacher A. **Intranasal flu vaccine protective against seasonal and H5N1 avian influenza infections.** PLoS One. **2009**;4(4):e5336.

Alsharifi M, Müllbacher A, Regner M. Interferon type I responses in primary and secondary infections. Immunol Cell Biol. **2008**;86(3):239-45. Review.

Müllbacher A, Lobigs M, Alsharifi M, Regner M. **Cytotoxic T-cell immunity as a target for influenza vaccines.** Lancet Infect Dis. **2006**;6(5):255-6.

Alsharifi M, Lobigs M, Blanden R, Regner M, Lee E, Koskinen A, Müllbacher A. **Exhaustion of type-I Interferon following an acute viral infection.** The Journal of Immunology. **2006**, 177: 3235–3241.

Alsharifi M, Lobigs M, Regner M, Lee E, Koskinen A, Müllbacher A. **Type-I interferons, in response to viral infection, trigger systemic, partial, lymphocyte activation.** The Journal of Immunology, **2005**, 175: 4635-4640.

## **Opportunities for Honours and PhD students:**

### **Cross-Protective influenza vaccine.**

Protection against re-infection with homotypic influenza virus is mediated primarily by neutralizing antibodies but recovery from newly arisen influenza virus infections requires cytotoxic CD8<sup>+</sup> T (Tc) cells. While neutralizing antibodies target mainly the viral surface glycoproteins (HA and NA), which are subject to frequent antigenic variation, influenza-immune Tc cells target the more conserved proteins, such as the viral nucleoprotein (NP) and matrix protein. Accordingly, any universal influenza vaccine should have the capability of inducing cross-protective Tc cell responses. We have reported that gamma-irradiated influenza A virus preparations can induce cross-reactive Tc cell responses and shown that a single intranasal administration of  $\gamma$ -H1N1 protects mice against lethal avian H5N1 and other heterotypic influenza A infections. potential projects for postgraduate research students would be in the areas of:

1. Cross-protective cytotoxic T cell responses induced by  $\gamma$ -flu.
2. The role of the cytolytic effector molecules in recovery from influenza infection.
3. Cross-protective antibody responses induced by  $\gamma$ -flu.
4. Recognition of  $\gamma$ -flu and the induction of cross-protective immunity.

### **Exhaustion of IFN-I response and the susceptibility to secondary infections.**

We have previously reported that type I interferon (IFN-I) response mediates systemic, partial lymphocyte activation which is evident by elevated expression of CD69 and CD86. Using avirulent strain of Semliki Forest Virus (SFV) as a model, we have found that induction of both IFN-I response and the associated lymphocyte activation to be dependent on virus viability as  $\gamma$ -irradiated SFV ( $\gamma$ -SFV) failed to induce either. We have also reported a period of exhausted IFN-I responses as a result of primary viral infections, which was associated with enhanced susceptibility to a secondary infection with an unrelated virus. Our aim is to investigate the underlying factors responsible for the deficiency in IFN-I responses following acute viral infections, and to address some therapeutic approaches to alleviate the period of the enhanced susceptibility. Interestingly, we found  $\gamma$ -irradiation of influenza virus, in contrast to that of SFV, did not abrogate the induction of IFN-I. Thus, IFN-I responses of two unrelated ssRNA viruses and their  $\gamma$ -irradiated counterparts will be investigated to establish a model to study the underlying factors responsible for the deficiency in IFN-I responses. potential projects for postgraduate research students would be in the areas of:

1. Induction of IFN-I responses by SFV and Flu and their  $\gamma$ -irradiated counterparts.
2. The consequences of the sub-optimal response to secondary viral infections.
3. The underlying factors for the deficient IFN-I response following an acute viral infection.
4. Possible therapeutic approaches to alleviate the enhanced susceptibility to secondary infections.