The Role of Oncogene in Mycobacteria-induced Antophagy in Human Macrophages

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Macrophages are the major immunocytes to initiate both innate and adaptive immune responses against Mycobacterium tuberculosis (Mtb), a causative agent of tuberculosis. Upon mycoabcteria infection, macrophages could eliminate the intracellular bacteria through different cell death pathways, including apoptosis and autophagy.

c-Myc is a transcription factor that regulates a variety of target genes and control different cellular functions such as proliferation and immune resposnse. Recently, our group revealed that c-Myc has a potential role in regulating the antimicrobial responses in macrophages.

Here we use BCG, a live attenuated strain of Mycobacterium bovis, which is similar to Mtb in antigenic composition, as a model to study the role of c-Myc in regulating mycobacteria-induced autophagy. We first investigated the role of c-Myc in BCG-induced LC3BII levels. Knocking down c-Myc by siRNA could decrease BCG-induced LC3BII levels. We found that BCG-induced autophagy is dependent on JNK and p38 and independent on PI3K or ERK pathways. And knocking down of c-Myc could significantly inhibit phosphorylation of p38. In conclusion, c-Myc may play a positive role in mycobacteria-induced autophagy in human macrophages.

Right Ventricular Mechanics in Adolescents and Young Adults Long-term After Repair of Coarctation of the Aorta

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Background: Alteration of right ventricular (RV) function has been found in patients with pressure-loaded left ventricles due to systemic hypertension and aortic stenosis. We tested the hypothesis that RV function may be altered in adolescents and adults with repaired coarctation of the aorta (CoA) and related to left ventricular (LV) mass.

Methods: Twenty-eight (15 males) patients with CoA, aged 23.7±6.5 years, at 20.6±5.4 years after surgical or catheter interventions and 28 (14 males) aged matched healthy controls were studied. Patients with significant residual CoA were excluded. M-mode, tissue Doppler imaging, and speckle tracking echocardiography were performed to assess LV mass and shortening fraction, anterior RV wall thickness, and RV myocardial tissue velocities and deformation.

Results: Systolic (p=0.14) and diastolic (p=0.32) blood pressure was similar between patients and controls. Compared with controls, patients had significantly greater LV shortening fraction (p=0.028), indexed LV mass (p=0.016), and indexed RV anterior wall thickness (p=0.012). With regard to RV function, patients had significantly lower tricuspid annular systolic (p<0.001) and early diastolic (p<0.001) velocities, isovolumic acceleration (p=0.004), global RV systolic longitudinal strain (p=0.03), systolic strain rate (p=0.012), and early (p=0.021) and late (p=0.012) diastolic strain rates than controls. Patients with an associated ventricular septal defect (n=6) requiring closure compared to those without had even lower tricuspid annular systolic (p=0.01) and early diastolic (p=0.041) velocities. For the whole cohort, LV mass correlated negatively with RV systolic strain rate (r=-0.27, p=0.045) and tricuspid annular early diastolic velocity (r=-0.40, p=0.002), while RV anterior wall thickness correlated negatively with tricuspid annular systolic (r=-0.42, p=0.002) and late diastolic (r=-0.40, p=0.003) velocities, and positively with e/a ratio (r=0.31, p=0.024).

Conclusion: RV systolic and diastolic function is impaired in patients late after repair of CoA and related to increased LV mass and RV thickness, even in the absence of residual CoA and systemic hypertension.

Investigating the Role of Interleukin-17A on Cytokines Production by Macrophages in Response to Bacterial Infections

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Interleukin-17A (IL-17A) has been shown to associate with a variety of infection diseases. In this study, we investigate whether IL-17A affects cytokines production of human peripheral blood-derived macrophages during *Mycobacteriun bovis* BCG or *Klebsiella pneumoniae* infection. We observed that IL-17A-treated macrophages exhibited suppressed productions of TNF-α and IL-6 in

response to BCG infection. The reduction of cytokines production was not associated with cell death. On the other hand, IL-17A promoted TNF-α and IL-6 production by macrophages during *K. pneumoniae* infection. Furthermore, IL-17A did not affect TNF-α production induced by LPS and Pam_3Cys, which are TLR4 and TLR2 agonists, respectively. The data suggest that the differential regulation of cytokines production by IL-17A requires whole bacterium infection.

HIV-1 Tat Dysregulation of KSHV Induced Immune Response Through the Production of IL-8

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Human immunodeficiency virus (HIV) causes acquired immunodeficiency syndrome (AIDS) and is a major health issue around the world. HIV is known to induce a number of pathological problems in AIDS patients via the trans-activator (Tat) protein that is expressed and released by infected cells. One of the most important function of Tat is the dysregulation of the immune response. IL-8 is a chemokine known to be highly expressed in AIDS patients and Tat plays a major role in its production. IL-8 increases the HIV transmission and replication rate; and plays a role in Kaposi's sarcoma associated herpesvirus (KSHV) infection, which is a major opportunistic pathogen that AIDS patients are at risk to. KSHV is also known to induce the expression of IL-8 in patients, and IL-8 is known to assist tumour development by increasing angiogenesis. In our study, we investigated the role that Tat may have in manipulating the expression of IL-8 induced by KSHV in primary blood monocyte derived macrophages (PBMac). The results showed that pretreatment of PBMac with Tat inhibited the expression of IL-8 induced by KSHV by approximately 40%. We also found that Tat was able to inhibit the phosphorylation of STAT-1 induced by KSHV, and the inhibition of STAT-1 phosporylation was related to the expression of IL-8 induced by KSHV. In conclusion, we found that Tat was able to manipulate the expression of IL-8 induced by KSHV in macrophages, and this inhibition of IL-8 expression was regulated through the STAT-1 related pathways.

Coping When a Child has Special Needs: Exploring the Function of Information from Community and Online Sources

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Background: Managing children with special needs can be physically and mentally demanding at times. Having adequate healthcare information can aid parents in their decision making.

Objective: This study recruited family members of children with special needs and professionals in relevant fields in Hong Kong. It aimed to explore the role and function of information from community and online sources with a specific focus on special parenting.

Methods: Qualitative focus group interviews were conducted in a semi-structured format. After obtaining informed consent, forty-nine participants were interviewed on issues of both general and online information seeking experiences. Two themes (information needs and sources of information supplementary to healthcare professional advice) were identified from the interviews.

Results: Results showed that caregivers need health- and service-related information to effectively manage the daily life of children with special needs. Having adequate information related to caregiving can foster parents' mental health. The Internet emerges as a new source for today's parents to seek information and identify "similar others" for support.

Conclusions: Lack of information and emotional support can harm the mental health and parenting skills of the parents especially those having children with special needs. Despite an increasing amount of health-related information in the Internet, parents'e Health literacy is critical for proper use and interpretation of online information. Conventional sources of information such as community groups are particularly important for parents with low eHealth literacy.