suggesting a mechanism for the crosstalk between BMP and GCN2.

Conclusion We have discovered in *Drosophila* that GCN2 activation modulates BMP signalling. This effect is mediated, at least in part, by the downstream transcription factor ATF4, which inhibits the phosphorylation of MAD (insect SMAD1). Our findings indicate that this pathway is conserved between insects and mammals and this model may shed light on the pathogenesis of PAH and PVOD.

S87 DEFICIENCY OF TOLL-LIKE RECEPTOR 3 (TLR3) EXACERBATES PULMONARY HYPERTENSION IN MICE

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Introduction The mechanisms regulating aberrant vascular remodelling in pulmonary arterial hypertension (PAH) are poorly understood and treatments targeted at halting or reversing this process are lacking. Toll-like receptor 3 (TLR3) is a viral sensor and more recently has been established as a sensor of endogenous damage signals, responding to mRNA released by damaged cells. TLR3 signalling induces pro- and anti-inflammatory cytokine production and regulates inflammation-associated apoptosis and tyrosine kinase signalling. In a model of systemic arterial injury, TLR3 signalling was shown to modulate neointimal remodelling in a protective manner. TLR3 is also expressed in pulmonary artery smooth muscle (PASMCs) and endothelial cells (PAECs). We therefore hypothesised that TLR3 would play roles in pulmonary vascular remodelling.

Methods TLR3-deficient (TLR3^{-/-}) or wild-type C57BL/6 (WT) mice were exposed to hypoxia (10% Oxygen) and given Sugen 5416 (weekly 20 mg/kg subcutaneous injections) or maintained in normoxic conditions for 3 weeks. Haemodynamic (cardiac catheterisation and echocardiography) and histological assessments were performed after 3 weeks. Human PASMCs were serum-starved before stimulation with PDGF or poly(I:C) and proliferation was assessed after 72 hours.

Results TLR3^{-/-} mice developed a markedly exaggerated phenotype of PAH in response to Sugen/Hypoxia with increased right ventricular systolic pressures (WT 51.6 mmHg $\pm$ 4.6 vs. TLR3^{-/-} 73.0 mmHg $\pm$ 6.8; $p < 0.05$, mean $\pm$ SEM, $n = 6$), increased muscularisation of small pulmonary arteries and reduced right ventricular cardiac output (WT 424.2 RVUmin⁻¹ $\pm$ 84.2 vs. TLR3^{-/-} 283.3 RVUmin⁻¹ $\pm$ 18.4, mean $\pm$ SEM, min $n = 6$) after 3 weeks. Poly(I:C) suppressed PDGF-induced PASMC proliferation in a dose-dependent manner.

Conclusions We have shown that mice deficient in TLR3 develop a markedly exaggerated haemodynamic pulmonary hypertension phenotype and human PASMC proliferation is suppressed by the TLR3 ligand, poly(I:C). Together these data imply that TLR3 signalling in disease mediates a protective phenotype in keeping with that observed in systemic vascular remodelling, and identify a protective pathway potentially amenable to therapeutic targeting.

Tuberculosis: From Screening to Side Effects

S88 NEITHER UK TUBERCULOSIS INFECTION TESTING GUIDELINE APPEARS COST-EFFECTIVE IN A CONTEMPORARY HIV INFECTED POPULATION

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UK guidelines advise testing for latent tuberculosis infection (LTBI) in people with known HIV. Both National Institute for Health and Care Excellence (NICE) 2011 and 2016, and British HIV Association (BHIVA) guidelines use targeted testing, in comparison to those from other countries, notably the United States. None of these have been compared for cost-effectiveness in a contemporary HIV population.

Abstract S88 Table 1 Costs for selected strategies, discounted cost/case prevented and cost/QALY gained compared to no testing and last (non-dominated) strategy

Strategy	Total cost of strategy per 10,000 people living with HIV	Cases TB prevented (discounted)	QALYs gained compared to no testing (discounted)	Cost/case averted	Cost/QALY compared to no testing	Incremental cost/QALY compared to last strategy
BHIVA 2011	£749,274	2.28	1.28	£21,371	£37,952	EXTENDED DOMINANCE
TST in BA	£749,660	3.9	2.09	£12,566	£23,429	£23,429
TST in BA and MI	£761,797	4.49	2.43	£13,614	£25,218	EXTENDED DOMINANCE
NICE 2011	£788,037	1.11	0.63	£78,429	£139,281	DOMINATED
IGRA in BA	£812,048	6.83	3.85	£16,314	£28,971	EXTENDED DOMINANCE
IGRA in BA and MI	£865,959	9.06	5.1	£18,250	£32,410	EXTENDED DOMINANCE
IGRA in all	£1,056,702	10.17	5.72	£35,030	£62,209	EXTENDED DOMINANCE
NICE 2016	£1,058,522	10.17	5.72	£35,234	£62,571	DOMINATED
TST&IGRA in all	£1,219,154	10.99	5.88	£47,166	£88,139	EXTENDED DOMINANCE
TST&IGRA&CXR&IS in all	£1,999,789	20.58	10.44	£63,142	£124,393	EXTENDED DOMINANCE

BA - Black African, BHIVA - British HIV Association, CXR - chest X ray, IGRA - Interferon-gamma release assay, IS - induced sputum, MI - middle [TB] incidence countries, NICE - National Institute of Health and Care Excellence, QALY - Quality adjusted life year, TB - tuberculosis (includes active disease and subclinical tuberculosis cases), TST - tuberculin skin test.