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Title: Genetic predisposition to RSV infection and associated respiratory morbidity in preterm infants

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Body: Introduction: Prematurely born infants who had respiratory syncytial virus (RSV) lower respiratory tract infections (LRTIs) may develop chronic respiratory morbidity. Aims and objectives: To test the hypotheses that prematurely born infants have a genetic predisposition to develop RSV LRTIs which is influenced by premorbid lung function and a genetic predisposition to chronic respiratory morbidity and/or reduced lung function following an RSV LRTI. Methods: After maternity unit discharge, nasopharyngeal aspirates (NPAs) were obtained when the infants had an LRTI in the community or in hospital. Chronic respiratory morbidity was assessed using respiratory health related questionnaires and parent completed diary cards. Lung function was measured at 36 weeks postmenstrual age (PMA) and at one year corrected age. Blood or buccal swabs were obtained and DNA tested for eleven single nucleotide polymorphisms (SNPs). Results: A SNP in ADAM33 was associated with an increased risk of developing RSV LRTIs, but no significant differences were found in any of the lung function results at 36 weeks PMA between the ADAM 33 genotypes. SNPs in several genes were associated with increased chronic respiratory morbidity (IL10, NOS2A, SFTPC, MMP16 and VDR) and abnormal lung function at one year corrected age (MMP16, NOS2A, SFTPC and VDR) in infants who had had RSV LRTIs. Conclusions: Prematurely born infants have a genetic predisposition to developing symptomatic RSV LRTIs, which is not influenced by premorbid lung function abnormalities, and a genetic predisposition to chronic respiratory morbidity following RSV LRTIs.