and a high risk of amyloidosis. Modifiers also affect the FMF phenotype. Recently, a Turkish study showed that patients with the G138 polymorphism in exon 2 are more prone to develop amyloidosis. MICA, the Major Histocompatibility Complex class I chain-related gene A, and SAA are two non-MEFV modifier loci. The impact of M694V homozygosity on the age at onset is aggravated if patients also inherited MICA A9, whereas MICA A4 is associated with a milder form of the disease. Renal amyloidosis is enhanced in patients with the SAA-1 alpha/alpha genotype and in males, each factor acting independently.

The MEFV mRNA is about 4kb length. It is expressed in mature neutrophils, eosinophils, monocytes, and in some cancer cell lines. It is upregulated *in vitro* by some proinflammatory mediators such as IFN. The protein encoded by MEFV was called Marenosttrin by the French group, and Pyrin by the International consortium. It is a 781 amino acid protein of a predicted 86 kd molecular weight. The predicted rodent proteins have considerable homology with humans, but do not have an intact C terminal domain, in which most FMF-associated mutations have been found in humans! It has been thought for a while that Marenosttrin/Pyrin was a transcription factor, because of the presence of two nuclear localisation sites in the gene sequence, and because of the presence of a zinc-finger motif. But immunofluorescent staining studies showed that unexpectedly, the protein was cytoplasmic and colocalized with microtubules. These data have been challenged recently by the finding of a deleted isoform that specifically binds to the nucleus. Thus identification of the MEFV function remains a difficult task.

Infection in paediatric rheumatology – Friday 15 June, 14.00-15.30/Forum Hall

SP0075 MACROPHAGE ACTIVATION SYNDROME AND SYSTEMIC JIA

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Systemic JIA is characterised not only by arthritis, but also by systemic features such as intermittent fever, lymphadenopathy, hepato-splenomegaly, exanthema and serositis. The disease occurs predominantly in childhood. It often begins at a young age and usually has a serious outcome, although new therapeutic regimes like high dose methotrexate, cyclosporine-A and TNF- α blockade have improved the prognosis.

A serious complication of systemic JIA is the Macrophage Activation Syndrome (MAS), which is often triggered by infections and medicines like gold and sulfasalazine. MAS is characterised by persistent high fever, mild to serious derangements of liver cell functions, purpura, encephalopathy and disseminated intravascular coagulation. Laboratory investigations often show a leucocytopenia, thrombocytopenia and anaemia in combination with elevated levels of bilirubin and hepatic enzymes. In the bone marrow and other organs like the lymphglands, liver and brain, haemophagocytizing histiocytes are demonstrable. Although they are not specific for MAS, the presence of haemophagocytizing histiocytes together with the other specific clinical symptoms enables the clinician to make the diagnosis.

MAS is a very serious, life-threatening complication of systemic JIA, which has to be treated with high dose corticosteroids, often in combination with cyclosporine. Even with this regimen the mortality rate is high.

Familial Haemophagocytic Lymphohistiocytosis (FHL), a congenital disease of childhood, is also characterised by haemophagocytosis. Recently, a defect in the perforin gene was found in patients with FHL. Because of the resemblance with MAS in systemic JIA, we have also investigated the perforin expression on cytotoxic CD8⁺ effector T-cells and NK-cells. We find a decreased expression of perforins in systemic JIA, which could play a role in the pathogenesis of the disease.

Osteoarthritis – Wednesday 13 June, 14.00-16.00/Forum Hall

SP0005 RISK FACTORS FOR OSTEOARTHRITIS

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Osteoarthritis (OA) is not a disease or a single condition. Diverse observations suggest that it may reflect the repair process of synovial joints. Sites commonly targeted by symptomatic OA include finger joints, knees and hips. These sites have different risk factors for development of structural OA. Different risk factors may relate to structural progression and outcome. Risk factors for pain and disability (such as muscle weakness and adverse psychosocial factors for the knee) may also differ from those relating to structural change.

Risk factors for development of structural OA are divisible into general constitutional factors and local, predominantly biomechanical factors. Important constitutional factors include heredity and ageing (all sites); Caucasian ethnicity (hip); female gender (hands, knees); and obesity (knees). Overt trauma can predispose to OA, but so may specific repetitive activities relating to occupational and recreational usage (eg football, knee bending while load carrying – knee OA; farming – hip OA). Possible negative associations include osteoporosis (hip >knee) and smoking (knee >hip). The role of poor nutrition (especially low antioxidants and vitamin D) in development and progression of knee and hip OA merits further study.

The genetic study of OA promises important insights into pathogenesis. A strong genetic contribution to OA of the hand, knee and hip has been shown using strategies such as: classic twin study; estimation of the relative risk of OA in siblings of OA patients; and segregation analysis of clustering of OA within families. Through candidate and genome wide association studies of affected sibling pairs, genetic associations are now being identified on several chromosomes (notably 2q, 11 and 16) and it is hoped that predisposing genes will shortly be identified. Inheritance is likely to be polygenic and to involve common polymorphisms, each with a relatively low attribution to OA. The next stage will be gene-gene and gene-environmental interaction studies to determine how individual genes and constitutional or environmental factors interrelate to cause OA and to modify its progress.