SP0012 THE HYGIENE HYPOTHESIS IN AUTOIMMUNITYJean-Francois Bach. *Institut de France, Académie des Sciences, Paris, France*

Background and Aims: The frequency of autoimmune diseases has increased significantly in recent decades in developed countries. The hygiene hypothesis provides a possible explanation for this increase. The hypothesis is based on the observation of a concomitant decrease in the frequency of infectious diseases and an increase in the frequency of autoimmune diseases. It is also based on the geographical disparity in the frequency of autoimmune diseases, much more frequent in the north than in the south of the northern hemisphere, a disparity that is not explained by genetics.

Method: The disease frequency which is very low in southern countries increases from the first generation among subjects migrating northward. The causal relationship between the decline in infections and the increase in autoimmune diseases remains to be proven. Most of the evidence is based on spontaneous experimental models of autoimmune diseases that show the higher frequency of these diseases in a clean sanitary environment and their prevention through the administration of various bacteria, viruses or parasites.

Results: The underlying mechanisms are beginning to be revealed. An important place is given to pathogens and more particularly to their TLR ligands. Some arguments suggest that commensal bacteria in the intestinal microbiota also play a role. At the cellular level, the stimulation of certain regulatory cells and more particularly those producing TGF beta is well documented.

Conclusion: These considerations are important for understanding the epidemiology and pathophysiology of autoimmune diseases but can also provide new guidance on their treatment and especially their prevention. The problem is, however, complicated by the fact that the theory applies to varying degrees depending on the disease, for instance more in systemic lupus erythematosus than rheumatoid arthritis.

Disclosure of Interests: None declared

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WEDNESDAY, 12 JUNE 2019

14:15:00 – 15:45:00

Pharmaceutical pipeline in OA**SP0013 GROWTH FACTORS AND CARTILAGE: FROM MECHANISMS TO DMOADS**Marc Hochberg. *University of Maryland, School of Medicine, United States of America*

Background: Growth factors are biologically active molecules that can stimulate cellular division, growth and differentiation and, in articular cartilage, can regulate development, homeostasis and regeneration of matrix. These anabolic factors can stimulate synthesis of proteoglycans, aggrecan and type II collagen, induce mesenchymal stem cell (MSC) proliferation and drive differentiation of MSCs into chondrocytes and decrease catabolic effects of cytokines and matrix metalloproteinases (MMPs). Growth factors would not, however, be expected to have a direct analgesic effect in patients with symptomatic knee osteoarthritis.

Objectives: To review the role of growth factors in articular cartilage, identify specific growth factors and review data from phase 1 and 2 studies of selected growth factors in subjects with knee osteoarthritis.

Methods: A PubMed search was performed using key words "cartilage or chondrocyte" and "growth factor". The search included both original manuscripts and review articles as well as clinical trials but was limited to English language. From these searches, I selected review articles and clinical trials and excluded articles that solely examined molecular mechanisms of action of growth factors on chondrocytes.

Results: Growth factors for articular cartilage include molecules in the transforming growth factor- β (TGF- β) superfamily (including TGF- β 1, bone morphogenic protein (BMP)-2 and BMP-7), insulin-like growth factor-I, fibroblast growth factor (FGF) family (including FGF-2 and FGF-18), platelet-derived growth factor (PDGF) and Wnt ligands as well as platelet rich plasma (PRP).

Conclusion: Data will be presented from phase 1 and 2 studies of rhFGF-18 and SM-04690, a Wnt signaling inhibitor, that demonstrate proof-of-concept and early efficacy of these growth factors for structure modifying effects in subjects with knee osteoarthritis (OA).

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Disclosure of Interests: Marc Hochberg Shareholder of: BriOri Biotech, Theralogix LLC., Consultant for: Bristol Myers Squibb, Eli Lilly, EMD Serono, Novartis Pharma AG, Pfizer Inc., Samumed LLC, Symic Bio Inc., Theralogix LLC, Tissue-Gene Inc., TLC Biopharmaceuticals, Inc., Zynherba, Galapagos, IQVIA, Hoffman LaRoche.

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14:15:00 – 15:45:00

What's new: Latest news on biological treatment**SP0014 THE LATEST NEWS ON BIOSIMILARS TREATMENT**Jonathan Kay. *UMass Memorial Medical Center and University of Massachusetts Medical School, Division of Rheumatology, Department of Medicine, and Department of Population and Quantitative Health Sciences, Worcester, Massachusetts, United States of America*

Biologic medications have revolutionized the treatment of many rheumatologic diseases, but their high cost often limits patient access to these effective treatments. Biosimilars are legitimate copies of biopharmaceuticals, which no longer are protected by patent, that have undergone rigorous analytical and clinical assessment in comparison to their reference products and have been approved by a regulatory authority in a highly regulated area according to a specific pathway for biosimilar evaluation. In 2005, the European Medicines Agency (EMA) established a pathway for the review and approval of biosimilars and, one year later, approved the human growth hormone Omnitrope® as the first biosimilar. As of March 2019, 56 of 60 biosimilars approved by the EMA were commercially available in the European Union, of which 6 were of rituximab and 15 were of TNF inhibitors to treat rheumatologic diseases.

Commercially available lots of a reference product are not identical to one another. All biologic medications are subject to normal batch-to-batch variability and are monitored to ensure that this variation is within "proven acceptable ranges" so that patients are not subjected to risks of lesser safety or efficacy. Since biosimilars have been compared extensively to their reference products and been shown to have highly similar structure, equivalent efficacy, and comparable safety, an approved biosimilar can be considered to be like another batch of its reference product. Thus, patients need not be apprehensive about using an approved biosimilar in place of its reference product.

The "nocebo effect" refers to the misattribution of bodily symptoms to a medication and may result in discontinuation of a treatment that is not actually causing the perceived symptoms. Studies have suggested that the nocebo effect may result in discontinuation of treatment with a biosimilar because of subjective perceptions. This may be addressed by providing encouragement and reassurance through education and open collaborative discussion between providers and patients. By taking this approach to counseling patients, the rate of biosimilar discontinuation may be reduced.

The NOR-SWITCH study demonstrated that patients with inflammatory diseases controlled on treatment with reference infliximab do not experience greater worsening of disease activity when switched to biosimilar infliximab CT-P13 than when continued on treatment with the reference product. Thus, when the cost of the biosimilar is significantly lower than that of its reference product, substituting the biosimilar for the reference product may provide an economic advantage with no loss of clinical benefit. In Norway, where there is an annual "winner takes all" competitive tender process for hospital administered medications, the price of biosimilar infliximab in 2015 was 69% lower than that of its reference product. Thus, in most countries, it is safe, effective, and cost-effective to switch to a biosimilar. However, competition from biosimilars has occasionally driven down the price of a reference product, as in Sweden where the price of reference adalimumab was reduced by 80% in 2018 and became lower than that of adalimumab biosimilars.

The availability of lower-priced biosimilars should decrease the cost of treating patients by introducing market competition. Biosimilars should be more readily available to patients for whom the reference product had been inaccessible because of cost. Greater global access to effective biologic medications should reduce disability, morbidity, and mortality associated with rheumatologic diseases.

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