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Morphological substrates in Rheumatoid Arthritis pathogenesis

K.J. van Zwieten¹, I. Lambrichts¹, B.S. de Bakker², L. Kosten¹, S. De Munter¹

¹*Department of Anatomy, Morphology, BioMed Institute, University of Hasselt, University Campus, Agoralaan, Building D, B 3590, Diepenbeek, Belgium*

²*Department of Anatomy, Embryology and Physiology, Academic Medical Center, Meibergdreef 15, 1105 AZ Amsterdam, The Netherlands*

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Introduction, Material and Methods. From a molecular-developmental point of view, in the exoskeleton joints of insects, high Notch-signaling levels promote ball production whereas low levels are required for socket production [1]. In humans however, the development of the “matching” convex-concave articular surfaces in e.g. finger synovial joints proceeds in a quite different way. To gain more insight into the morphogenesis of synovial joints, as well as into chronic joint diseases like Rheumatoid Arthritis (RA), we first surveyed finger joint ontogeny from early developmental stages. High Resolution Magnetic Resonance Imaging (HR-MRI) of the adult proximal interphalangeal (PIP) joint in an otherwise normal anatomical specimen of the finger was then analyzed. We finally investigated the microscopic anatomy of part of the PIP joint capsule, namely its Proper Collateral Ligament (PCL)

Observational results. From the seventh week of embryonic development, digital rays successively show local mesenchymal condensation, interphalangeal joint interzone development, and joint space development [2]. These interzones are characterized by intense staining areas. Before the joint spaces become recognizable, the interphalangeal interzones already indicate convexities at the future “ball”-side of each joint, and concavities at its future “socket”-side. By their broadness, these areas also prefigure the development of joint capsules. Later in ontogeny, increasing incongruences of the PIP joint’s articular surfaces are more or less “compensated” by the development of wedge-like vascularized synovial folds. Dorsal and palmar, but also ulnar and radial synovial folds do persist in adult PIP joints, as HR-MRI slices clearly show. In synovial joints, the synovial membranes as well as their folds may be involved in auto-immune reactions leading to Rheumatoid Arthritis, the so-called “inside-out scenario” of Rheumatoid Arthritis [3]. This focused our attention on the micro-vascularity of finger joint capsules. PIP arteriography and microscopy demonstrated the presence of microvascular articular networks, perfectly fitting with this “inside-out” hypothesis. Arterioles and capillaries, accompanied by neurons and currently surrounded by connective tissues, pierce through the various collagenous fiber-bundles of the PIP joint’s Proper Collateral Ligament. Microvascular structures branch off at right angles to each other. By anti-200 kD Neurofilament Heavy Antibody staining, the neurovascular structures were also made visible in detail.

Results and Conclusions. In the PIP joint capsule, neurofilaments and lamellated corpuscles are observed, comparable with those present in human facet joints [4, 5]. Our study demonstrated these corpuscles in the PIP Proper Collateral Ligament for the first time. Supposedly acting as mechanoreceptors, they may also produce cytokines and substance P, a neuropeptide involved in pain [5]. As the PIP joints of fingers in particular show symptoms of Rheumatoid Arthritis at very early stages [3], these organs may therefore play a role in the pathogenesis of Rheumatoid Arthritis.

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