Priority Program 1468: Osteoimmunology – IMMUNOBONE – A Program to Unravel the Mutual Interactions between the Immune System and Bone

Speaker
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Aims and structure

The interdisciplinary project “Osteoimmunology – IMMUNOBONE – A Program to Unravel the Mutual Interactions between the Immune System and Bone” (SPP 1468 – IMMUNOBONE) was a priority program that was funded by the DFG for the first funding period of three years with a total volume of 6.8 million euro. At the beginning of 2013, SPP 1468 was positively evaluated for a second funding period for additional three years with a total volume of 7.1 million euro. The interdisciplinary consortium consisted of 20 groups of 15 different research institutions of osteologic orthopedics, rheumatology, and immunology.

Research

At the time of the initial application, osteoimmunology was a newly discovered field of research between immunology and bone biology. This field was stimulated in particular by the discovery of RANKL (receptor activator of NF-κB ligand). With the establishment of the SPP 1468, this field has expanded significantly, revealing new mechanisms in the mutual regulation of bone and immune system. The main interest was the regulation of bone mass and architecture by immune system and inflammation as well as the characterization of bone and bone marrow as an organ necessary for differentiation and survival of immune cells. The extensive results obtained in SPP 1468 show that the immune and skeletal systems interact closely at several levels.

An important aspect of osteoimmunology is the regulation of the skeletal system by cytokines. Among other things, new findings on previously unknown biological functions of RANKL in the context of breast cancer, osteopetrosis, and diabetes mellitus could be defined. Furthermore, new insights were gained into how cytokines, which play a central role in psoriasis, affect bone. These results provide new explanations for immunological bone changes in psoriasis that have direct clinical relevance as IL-17 inhibition is already used to treat psoriasis. A new role of the IL-23/IL-17 cytokine axis in the transition from autoimmunity to inflammation was also defined. In this context, completely new mechanisms of control of the skeletal system by autoimmunity emerged. Already within the first funding period, a link between autoimmune body production and bone resorption was discovered within the framework of a „bedside-to-bench approach“. It was shown that human autoantibodies against citrullinated proteins found in most patients with arthritis are strong inducers of bone resorbing osteoclasts and cause bone loss. These findings provided new insights into bone resorption in rheumatoid arthritis.

Within the framework of the SPP 1468, new mechanisms of the regulation of bone formation could be identified in addition to immune regulators of osteoclasts. Thus, it could be shown that the nuclear receptor PPARγ/δ from the group of peroxisome proliferator-activated receptors (PPARs) contributes to osteogenesis by regulating the RANKL expression of osteoblasts and thus represents an innovative approach for the development of new bone-building osteoporosis drugs. Furthermore, excessive bone formation in connection with arthritis was an area of research in SPP 1468. Within this program, the role of Wnt proteins and their antagonists in pathological bone formation in arthritis was investigated during both funding periods.

Within the consortium, new groundbreaking discoveries on the regulation of bone and inflammation by glucocorticoids were made, which form the basis for the development of cortisone drugs with low side effects, in particular preparations that take into account the single molecule function of glucocorticoid receptors. These findings play a central role, especially for inflammatory diseases such as arthritis, where inflammation and bone loss occur side by side. In the field of clinical research, the consortium was able to develop methods that made it possible to visualize immune bone interaction in patients with inflammatory diseases using high-resolution imaging techniques (high-resolution quantitative computed tomography). The data from these studies enabled a better understand-