

S20-3 **Discovery of a novel hyaluronic acid-MTX conjugate (DK226) for Osteoarthritis**

○Haruhiko SATO¹, Tatsuya TAMURA¹, Tadashi MORIKAWA²

¹Chugai Pharmaceutical Co.Ltd., ²Denki Kagaku Kogyo

Intra-articular injection of hyaluronic acid (HA) has been licensed worldwide for the treatment of osteoarthritis (OA). Joint pain and inflammation are major hallmark symptoms of OA. Current HA can reduce pain, but not fully control inflammation. Oral methotrexate (MTX) provides a very effective treatment for rheumatoid arthritis (anti-proliferative plus anti-inflammatory). However, systemic adverse events, such as pneumonitis, liver fibrosis and myelosuppression, are frequently associated. Intra-articular injected HA can accumulate in synovium and be incorporated into synovial cells.

We therefore designed HA-MTX conjugates to combine the efficacy of the two arthritic drugs (pain reduction & anti-inflammatory effect), avoiding the risk of MTX by introducing HA as a DDS carrier for MTX. Here we show the optimization of peptide, linker, binding ratio of MTX, molecular weight of HA. We also show the detail of scientific rationale and in vitro and in vivo experimental data of **DK226**.