

**27. Development of IgA nephropathy-like disease with deficient *N*-glycosylation of serum IgA in  $\beta$ -1,4-galactosyltransferase-I-deficient mice**

**Masahide Asano (Kanazawa University)**

IgA nephropathy (IgAN) is the most common form of glomerulonephritis worldwide and 30-40% of patients progress to renal failure 20 years after the onset of the disease in Japan. However, pathological molecular mechanisms of IgAN remain to be elucidated. Here we report that mice deficient in  $\beta$ -1,4-galactosyltransferase ( $\beta$ GalT)-I developed human IgAN-like glomerular lesions with IgA deposition, expanded mesangial matrix, and mesangial cell proliferation. Furthermore, they showed high serum IgA levels with increased polymeric forms. These features are consistent with the pathological diagnosis of human IgAN. Thus, the  $\beta$ 4GalT-I KO mouse is a novel pathological model for human IgAN. In humans, serum IgA1 with truncated *O*-glycans in its hinge region is suggested to be involved in the pathogenesis of IgAN. The polymeric and Gal-deficient IgA from the  $\beta$ 4GalT-I KO mouse tends to accumulate in the glomeruli. Since mouse IgA does not have *O*-glycans in its hinge region, our results strongly suggest that aberrant *N*-glycans as well as *O*-glycans of serum IgA play a pathological role in the development of IgAN.