DOCTORAL CANDIDATE:	Kine Marita Knudsen Sand
DEGREE:	Philosophiae Doctor
FACULTY:	Faculty of Mathematics and Natural Sciences
DEPARTMENT:	Department of Biosciences
AREA OF EXPERTISE:	Molecular biosciences
SUPERVISORS:	Inger Sandlie and Jan Terje Andersen
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DISSERTATION TITLE: *The FcRn-albumin interaction*

Albumin is the most abundant protein in the blood, and functions as a transporter of various compounds such as fatty acids, hormones and toxins. The long persistence in the bloodstream is a unique property of albumin, and its half-life is as long as 3 weeks in humans. Albumin has a long half-life because it escapes degradation inside the cells of the body due to a receptor-mediated recycling process involving the neonatal Fc receptor (FcRn). The receptor binds albumin in acidic vesicles and transports it back to the cell surface where it is released back to the bloodstream. The long half-life of albumin is increasingly exploited in design of new therapeutics to increase their time of action. Such albumin-based therapeutics enable both less frequent and lower dosing, which in turn will lead to more gentle treatment.

Kine M. K. Sand has in her doctoral thesis entitled “The FcRn-albumin interaction” shown on a detailed molecular level how albumin binds FcRn. She has dissected the interaction interfaces between the two proteins, and identified amino acids on both the receptor and albumin that are crucial for binding. This knowledge is further used to design novel albumin variants that are engineered to bind FcRn with considerable improved affinity. By cellular studies, Sand shows that FcRn is expressed on epithelial cells lining the mucosal surfaces, and that albumin can be transported across such cell layers in a process that requires FcRn. Furthermore, Sand demonstrates that engineered albumin variants with improved FcRn binding are transported more efficiently. The work of this thesis contributes to a more complete understanding of the interaction between albumin and FcRn, and pin-points that transport of albumin across epithelial cell layers does not only depend on FcRn, but that this biological process can be manipulated by molecular design of albumin variants with improved transport properties. The findings pave the way for a new strategy for delivery of albumin-based therapeutics across mucosal surfaces.