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Increased trans-glycosylation activity of hexosaminidases for synthesis of human milk oligosaccharides

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28/09-2017

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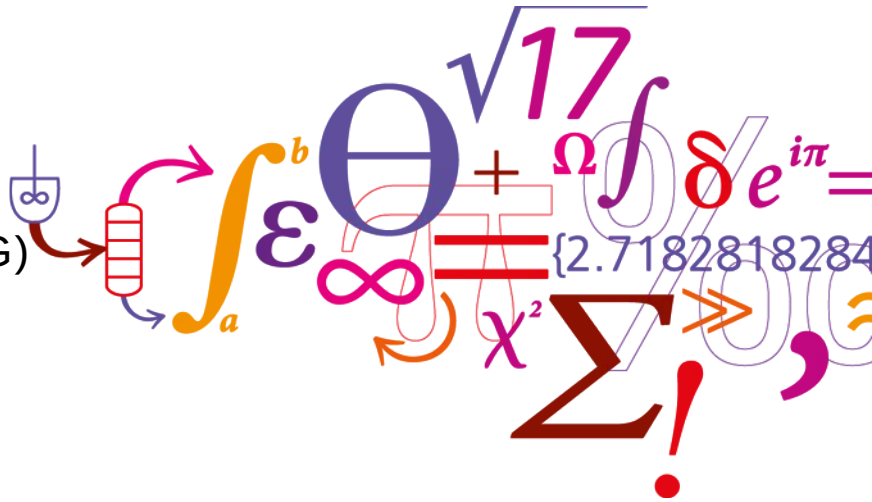
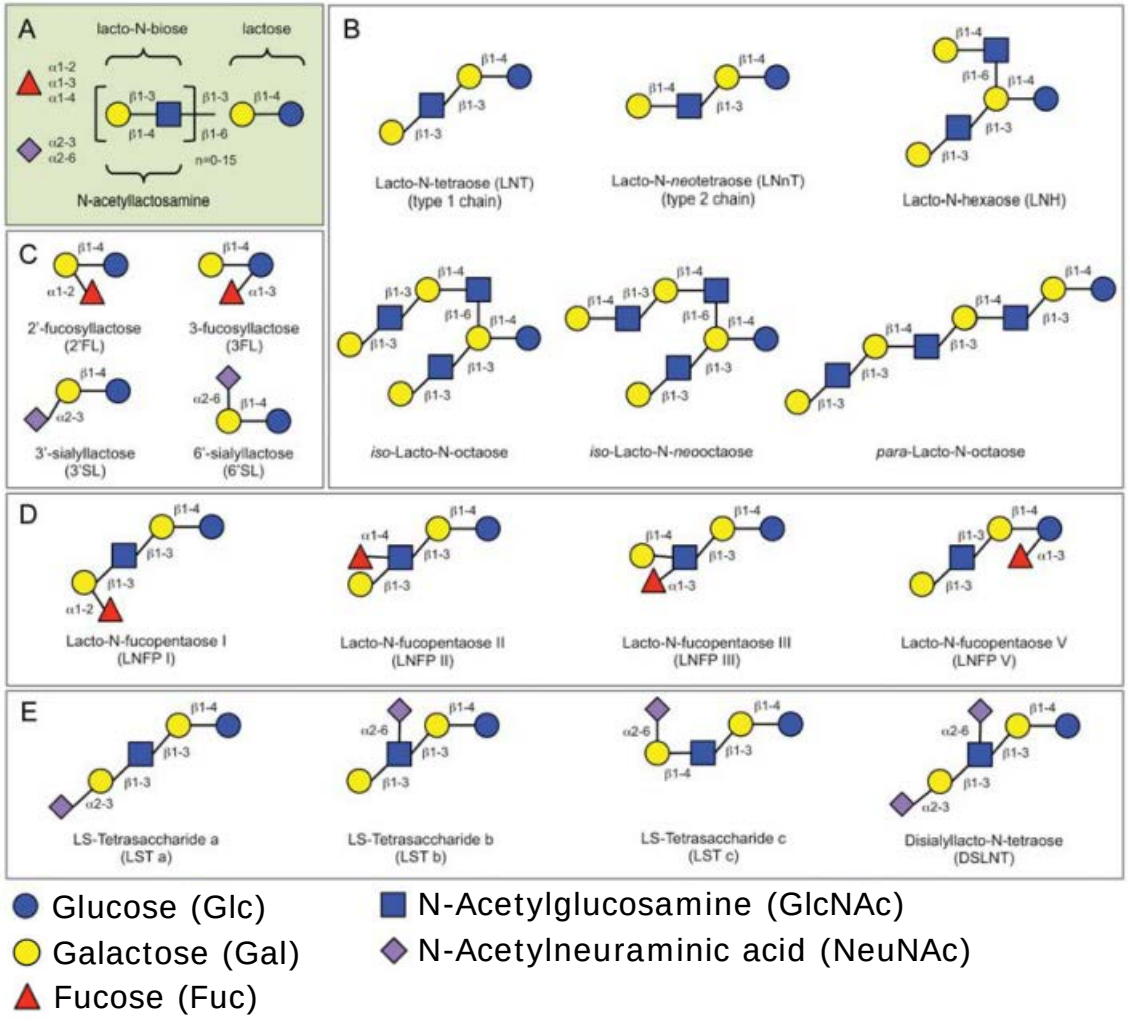


DTU Chemical Engineering
Department of Chemical and Biochemical Engineering

Human Milk Oligosaccharides (HMOs)

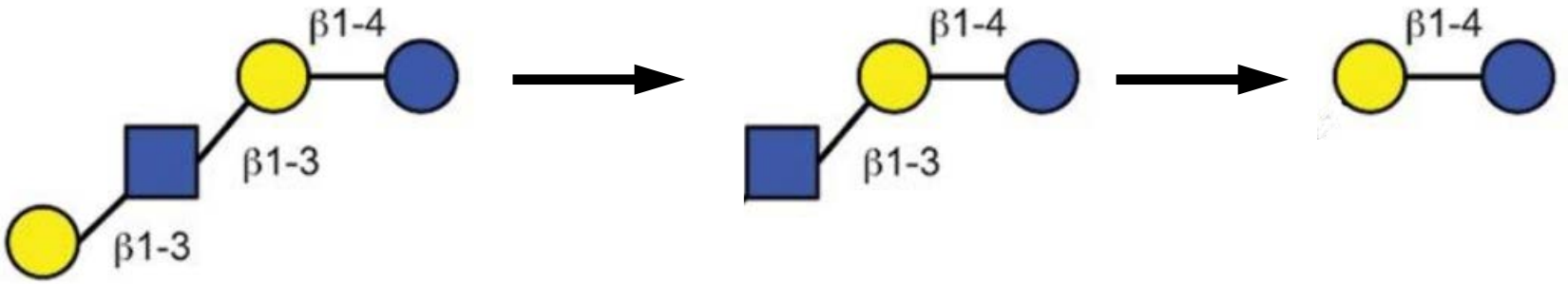


Postulated beneficial effects:

- Prebiotic
- Antiadhesive antimicrobial
- Modulatory on intestinal epithelial cell responses
- Immune modulatory
- Protective against necrotizing enterocolitis
- Nutritional for brain development

Bode (2012), Glycobiology 22:1147–1162.

Human Milk Oligosaccharides
- Retrosynthetic Aproach -



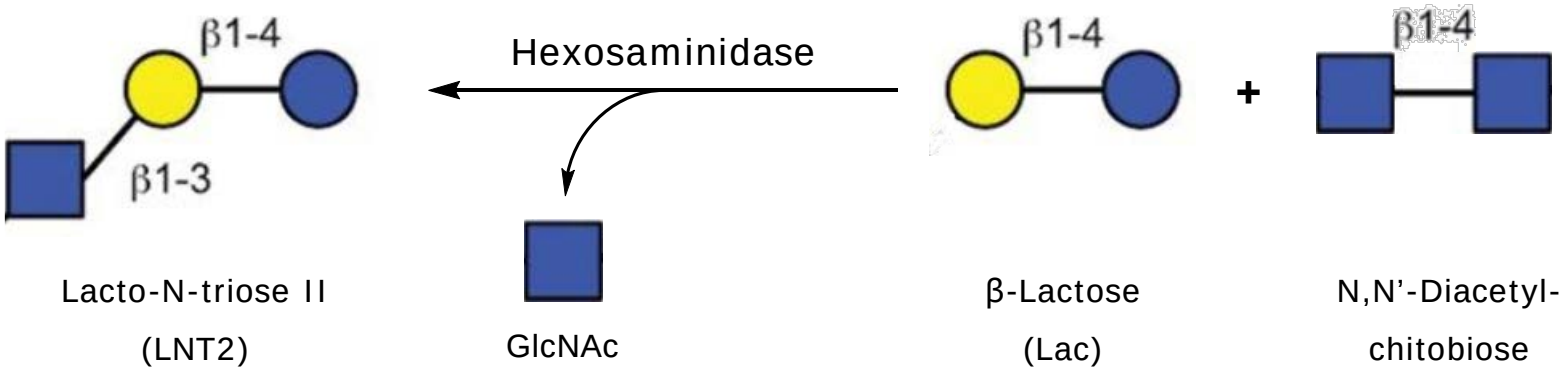
Lacto-N-tetraose (LNT)

Lacto-N-triose II (LNT2)

β-Lactose (Lac)

- Glucose (Glc)
- Galactose (Gal)
- N-Acetylglucosamine (GlcNAc)

Human Milk Oligosaccharides
- Retrosynthetic Aproach -



Yield after 3 h

HEX1: 4.0 %

HEX2: 5.5 %

(based on donor,

incl. all detected isomers)

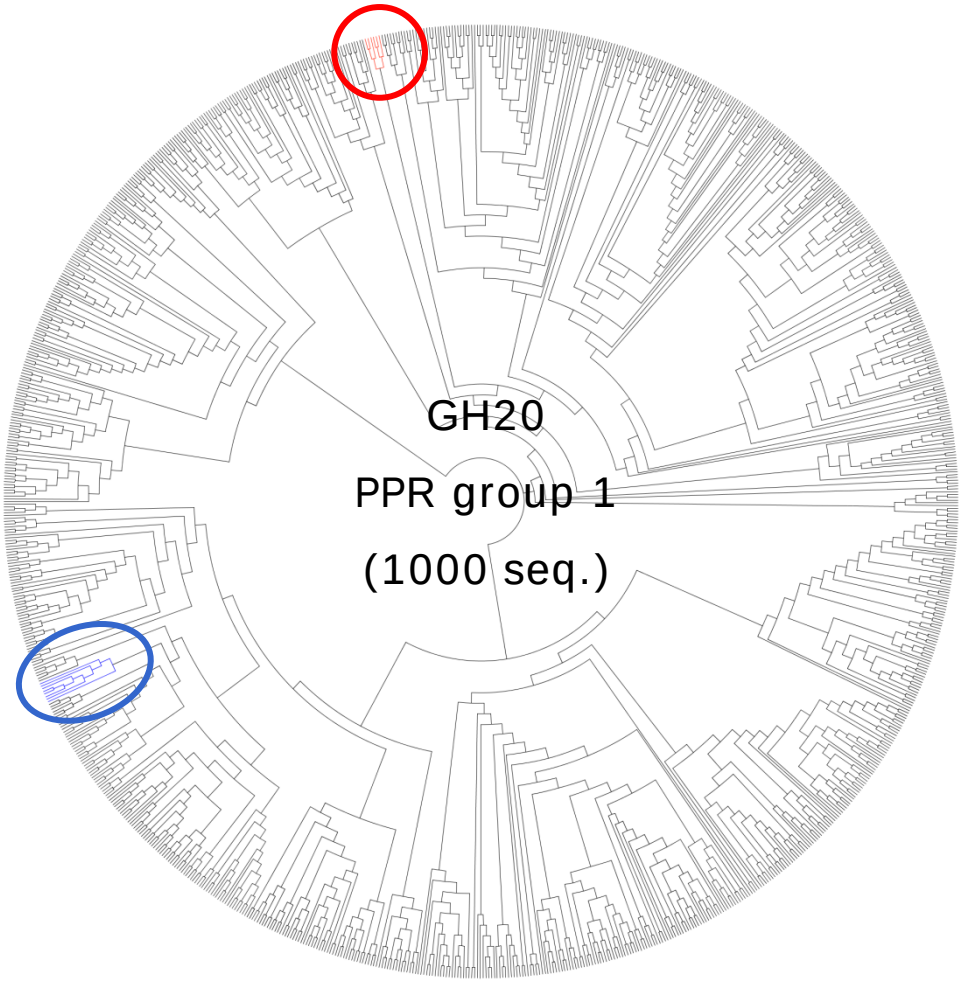
Glucose (Glc)

Galactose (Gal)

N-Acetylglucosamine (GlcNAc)

Nyffenegger, et al. (2015) Appl Microbiol Biotechnol 99:7997–8009.

Peptide Pattern Recognition (PPR)

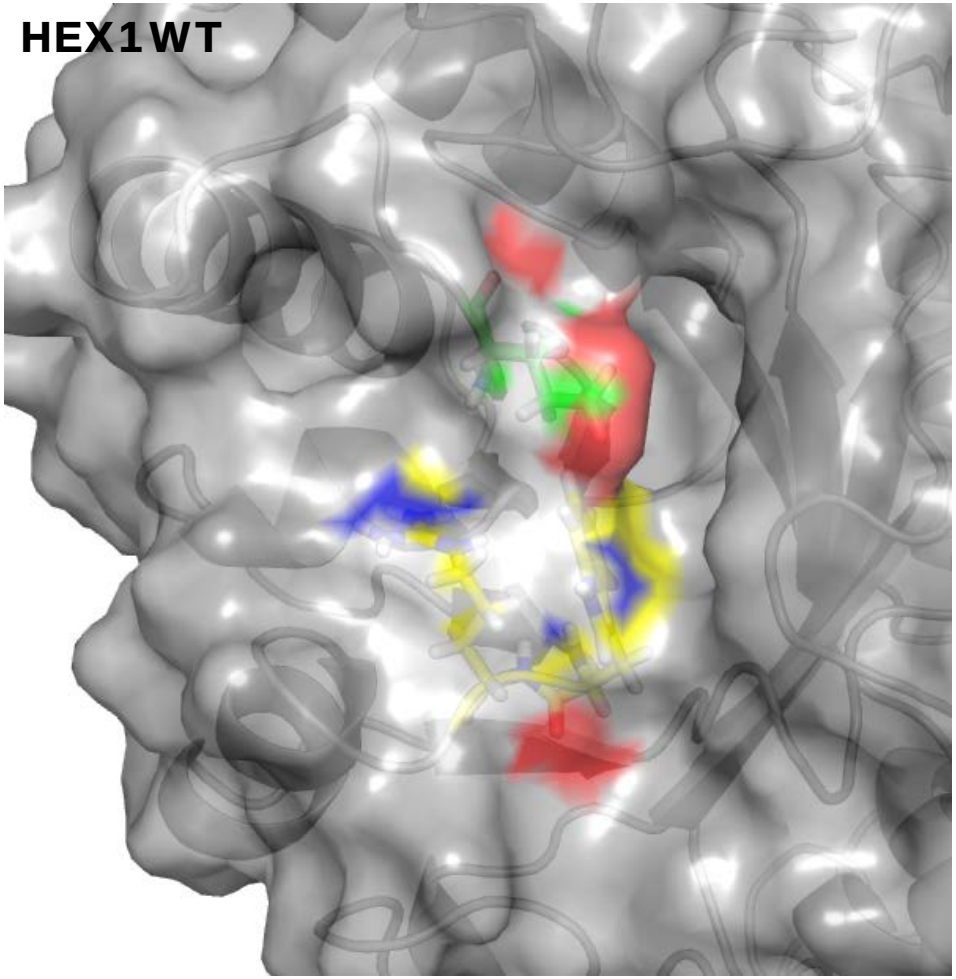


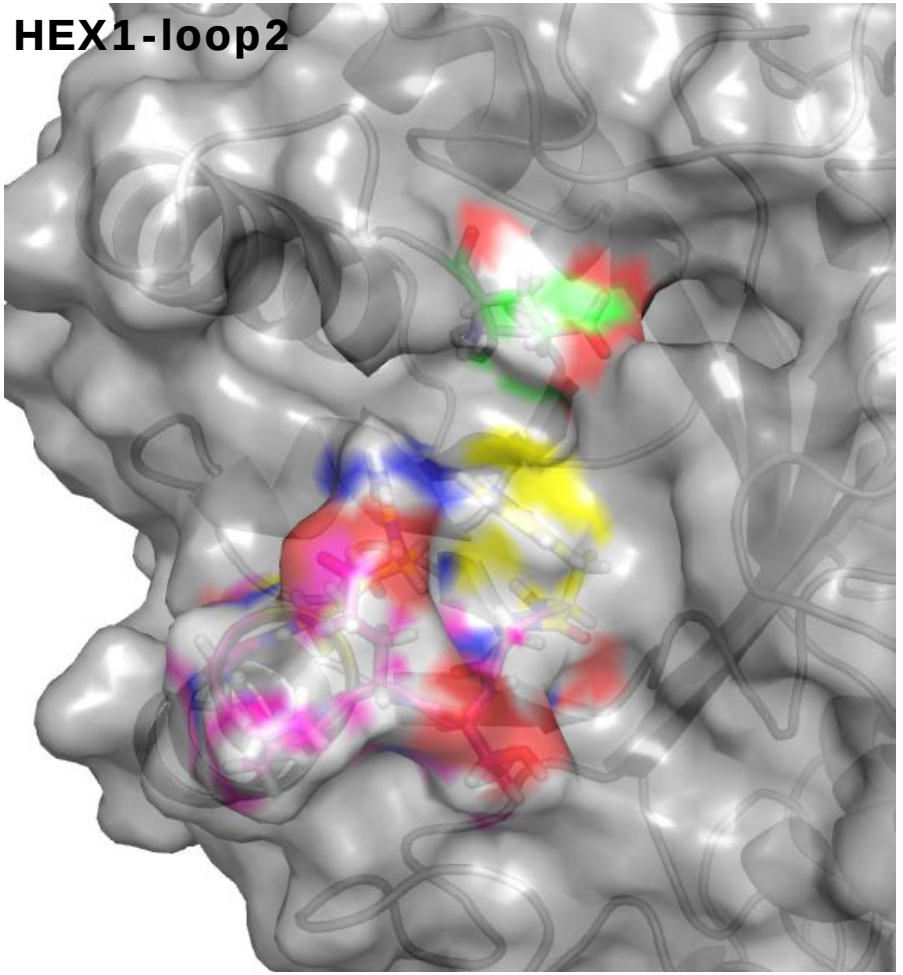
- Peptide Pattern Recognition in GH family 20 (3000 seq.) by Peter K. Busk
- HEX1 and HEX2 both in group 1 (1000 seq.)

Busk & Lange (2013) Appl Environ Microbiol 79:3380–3391.

Busk, et al. (2017) BMC Bioinformatics 18:214.

Homology modeling of loop engineered hexosaminidases

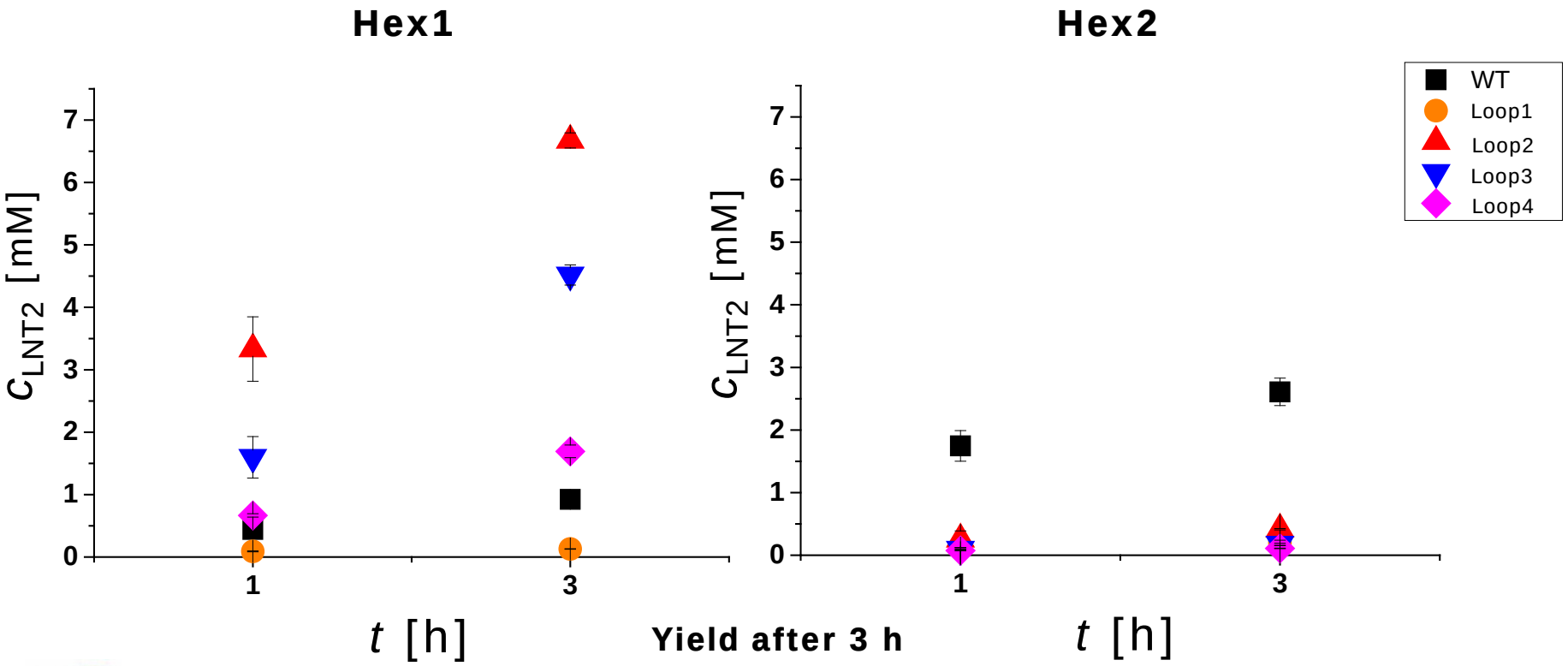




Modeling templates: 4C7D, 1JAK, 4C7G, 1M03, 1M04

Jamek, et al., manuscript submitted

LNT2 synthesis by loop engineered hexosaminidases



Yield after 3 h

HEX1-loop2: 17.0 %

(based on donor,

incl. all detected isomers)

Shariza B. Jamek

Jamek, et al., manuscript submitted

Acknowledgement

Shariza B. Jamek

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Jørn D. Mikkelsen

Anne S. Meyer

BIOENG in front of the Hasselbalch house (Snekkersten, DK)

OTTO MØNSTEDS FOND

Innovationsfonden