Structure-dependent effects of pectins on Toll-like receptor 2

Martin Beukema[1], Éva Jermendi[2], Henk Schols[2], Paul de Vos[1]

Background

Low-DM (methyl esterified) pectins from lemon have a direct, microbiota-independent, effect on the immune system in the small intestine by inhibiting TLR2/1 (Sahasrabudhe et al 2018). Moreover, high DM from lemon were also shown to activate TLR2 (Vogt et al. 2016). Both stimulation and inhibition of TLR2 may be instrumental in specific disease prevention.

Objective

We evaluated whether origin and chemical modification of pectins determines the immunomodulatory effect on TLR2 activation and TLR2/1 inhibition.

Characterisation of pectins

- All pectins consist mainly of uronic acid, galactose, arabinose, glucose and rhamnose and they differed in the degree of methyl esterification (DM) and blockiness (DB).

Table 1. Chemical characteristics of **orange pectin** samples.

			mol%					w/w%
Code	DM	DB	Rhamnose	Arabinose	Galactose	Glucose	Uronic acid	Total
DM64	64	37	0	7	7	1	84	86
DM59 (1)	59	25	1	3	7	2	87	89
DM59 (2)	59	22	1	3	9	3	84	83
DM59 (3)	59	17	1	3	8	1	88	87
DM57	57	18	1	2	8	2	86	87
DM53	53	28	1	3	8	2	86	81
DM32	32	35	1	3	6	1	89	87
DM30	30	17	1	2	7	2	87	83

Table 2. Chemical characteristics of **lemon pectin** samples.

			mol%					w/w%
Code	DM	DB	Rhamnose	Arabinose	Galactose	Glucose	Uronic acid	Total
DM75	75	60	0	2	4	0	93	86
DM60	60	55	0	1	5	0	93	81
DM45	45	58	0	0	5	0	94	73
DM22	22	85	0	0	3	1	95	73
DM7	7	116	0	0	3	0	95	68

Table 3. Chemical characteristics of **modified orange pectin** samples. Pectin DM64 was re-esterified to DM92 using acidic methanol and DM92 was de-esterified using alkaline to obtain pectins with DM63, DM50, DM32 and DM10.

			mol%					w/w%
Code	DM	DB	Rhamnose	Arabinose	Galactose	Glucose	Uronic acid	Total
DM92	92	43	0	0	7	1	91	74
DM63	63	20	0	0	6	2	92	80
DM50	50	24	0	0	6	2	91	79
DM32	32	28	1	0	6	2	92	75
DM10	10	60	1	0	6	1	91	74

Experimental approach

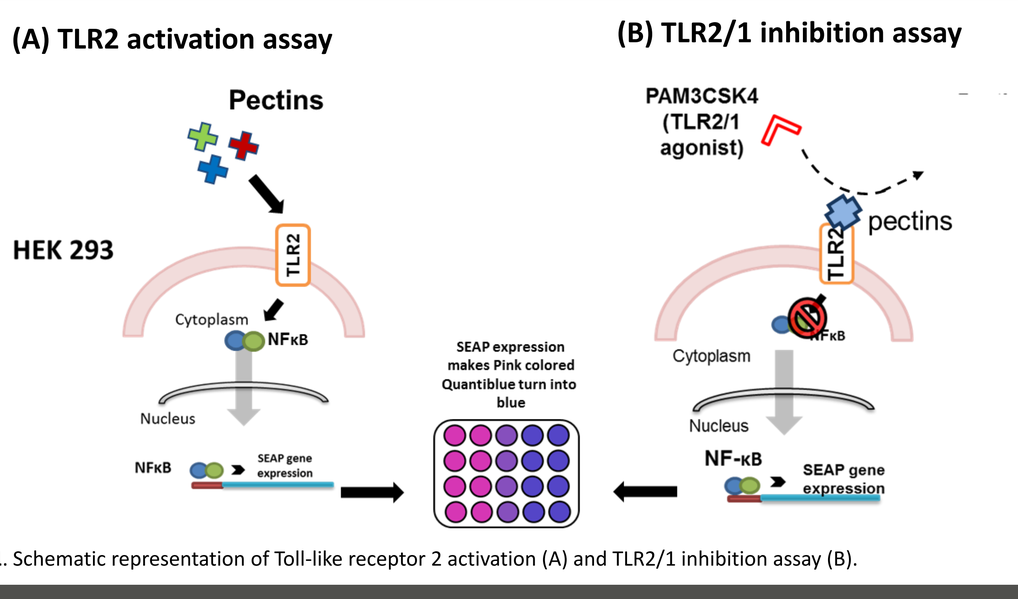

Figure 1. Schematic representation of Toll-like receptor 2 activation (A) and TLR2/1 inhibition assay (B).

TLR2 activation and TLR2/1 inhibition

- Chemical modification changes TLR2 immunomodulating properties.
- TLR2/1 was inhibited in a DM-dependent manner by lemon pectins only.

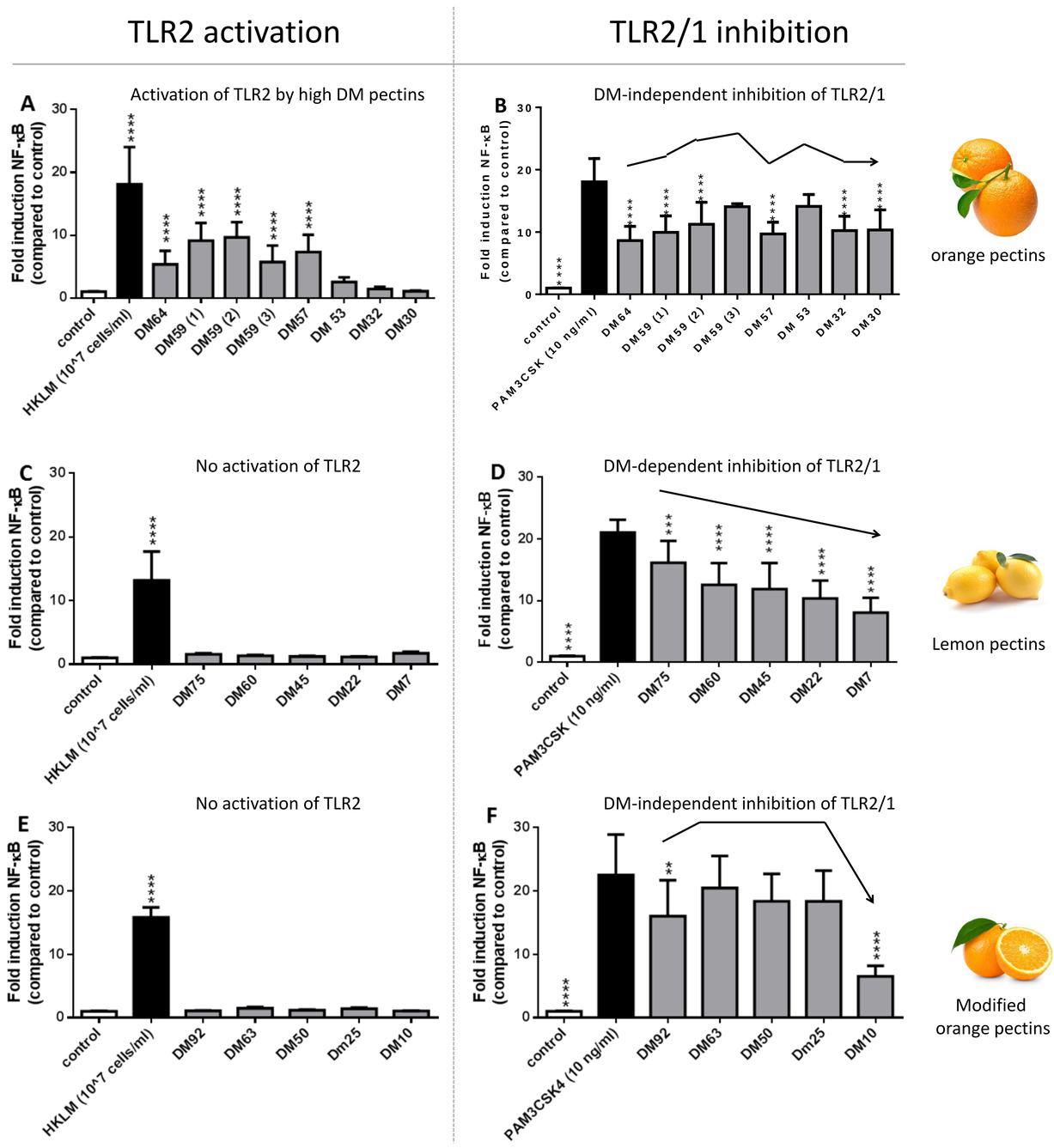

Figure 2. TLR2 activation and TLR2/1 inhibition by orange pectins (A,B), lemon pectins (C,D) and modified orange pectins (E,F). The statistical differences between control or PAM3CSK4 and pectin samples were quantified using the One-Way ANOVA test (*p<0.05, **p<0.01, *** p<0.001, **** p<0.0001) (n=4). HKLM = Heat Killed Listeria Monocytogenes; DM = degree of methylesterification.

Conclusion

- Chemical modification of pectins changes TLR2 activating and TLR2/1 inhibiting properties.
- TLR2/1 was only inhibited in a DM-dependent manner by lemon pectins, whereas the orange pectins inhibited TLR2/1 in a DM-independent manner. More structure dependent research has to be done to determine the exact characteristics of pectins that contribute to the immune function-effector relationships.

References

Sahasrabudhe NM, Beukema M, Tian L, Troost B, Scholte J, Bruininx E, Bruggeman G, van den Berg M, Scheurink A, Schols HA, Faas MM and de Vos P (2018) Dietary Fiber Pectin Directly Blocks Toll-Like Receptor 2–1 and Prevents Doxorubicin-Induced Ileitis. Front. Immunol. 9:383.

Vogt, L. M., Sahasrabudhe, N. M., Ramasamy, U., Meyer, D., Pullens, G., Faas, M. M., Venema, K., Schols, H. A. & de Vos, P. Apr-2016 In : Journal of Functional Foods.22, p. 398-407 10 p.

1. Division of Medical Biology
University Medical Center Groningen
Hanzeplein 1, 9713GZ Groningen
Contact: p.de.vos@umcg.nl www.umcg.nl

2. Laboratory of Food Chemistry
Wageningen University & Research
P.O. Box 17, 6700 AA Wageningen
Contact: henk.schols@wur.nl www.fch.wur.nl