Appendix III-b

Quantitave Data for 2'-FL and LNnT

Publications reporting quantitative data for individual HMOs

Quantitative data for individual HMOs have been reported in at least 39 publications by June 2017.[1-39] The table below provides the general overview on the reported studies, and on the main parameters of stratification of the data. In total, ~47 different individual HMOs have been quantified to date (while many more have been identified in structure)[40]; however, the data also clearly shows that a subset of around 10-15 individual HMOs make up the large majority of the biomass (>85%) in all milk samples analyzed, with 2'-FL being by far the most abundant HMO on average. The specific data for 2'-FL, and for LNnT, is presented in the next table on the following pages.

#	Reference	Milk group	Neutral	Acidic	Samples	Population	Birth term / preterm	Lactation day	HMOs quantified
01	Kunz et al. *Acta Pædiatr.* **1993**	pool	+	+	n/a	Europe	term	"mature milk"	8
02	Thurl & Sawatzki, *Anal. Biochem.* **1996**	**1**	+	+	1	Europe	term	"mature milk"	20
03	Chaturvedi et al. *Anal. Biochem.* **1997**	pool	+		50	Latin America	term	30-60	12
04	Coppa et al. *Acta Paediatr. Suppl.* **1999**	**1**	+	+	18	Europe	term	4, 10, 30, 60, 90	21
05	Nakhla et al. *Br. J. Nutr.* **1999**	pool	+		15	USA	*preterm*	0-33	10
06	Shen et al. *Anal. Biochem.* **2000**	pool		+	n.d.	USA	term	n/a	5
07	Erney et al. *JPGN* **2000**	pool	+		80 Asia 68 Europe 197 Lat. Amer. 36 USA		term	0-2, 3-10, 11-30, >31	9
08	Kunz et al. *Ann. Rev. Nutr.* **2000**	pool	+	+	4	Europe	term	2-19	8
09	Erney et al, *Bioactive Comp. Hum. Milk* **2001**	pool	+		268	America & Europe	term	1-100	9
10	Chaturvedi et al. *Glycobiol.* **2001**	pool	+		12	USA	term	"mature milk"	12
11	Sumiyoshi et al. *Br. J. Nutr.* **2003**	pool	+		16	Japan	term	4, 10, 30, 100	6
12	Martin-Sosa et al. *J. Dairy Sci.* **2003**	pool		+	12	Europe	term	1-4, 12-17, 28-32	7
13	Morrow et al. *J. Pediatr.* **2004**	pool	+		93	Latin America	term	1-100	4
14	Musumeci et al. *JPGN* **2006**	pool	+		53 Africa, 50 Europe		term	1, 2, 3	2
15	Bao et al. *Anal. Biochem.* **2007**	pool		+	13	USA	term	2-4, 12-67	12
16	Asakuma et al. *Biosci. Biotech. Biochem.* **2007**	pool		+	20	Japan	term	1-3	9
17	Asakuma et al. *Eur. J. Clin. Nutr.* **2008**	pool	+		12	Japan	term	1-3	10
18	Leo et al. *J. Chromatogr.* **2009**	pool	+		8	Samoa	term	5-10 and ">10"	11
19	Thurl et al. *Br. J. Nutr.* **2010**	**1-3**	+	+	30	Europe	term	3-90	20
20	Leo et al. *Biosci. Biotech. Biochem.* **2010**	pool	+	+	16	Samoa	term	5-10, 21-155	17
21	Asakuma et al. *J. Biol. Chem.* **2011**	pool	+		57	Japan	term	30-120	10
22	Coppa et al. *JPGN* **2011**	**1-4**	+		40	Europe	term	25-35	8
23	Gabrielli et al. *Pediatr.* **2011**	**1-4**	+	+	63	Europe	*preterm*	4-30	23
24	Galeotti et al. *Anal. Biochem.* **2012**	**1-4**	+	+	n/a	Europe	term	4-30	21
25	De Leoz et al. *J. Proteome Res.* **2012**	**1-4**	+	+	15	USA	*preterm*	"mature milk"	3
26	Totten et al. *J. Proteome Res.* **2012**	**1-4**	+	+	60	Africa	term	1-180	23
27	Bao et al. *Anal. Biochem.* **2013**	**1**	+		4	USA	term	3, 14-29	11
28	Smilowitz et al. *J. Nutr.* **2013**	pool	+	+	52	USA	term	90	10
29	Galeotti et al. *Electrophoresis* **2014**	**1-4**	+	+	9	Europe	term	4-30	16
30	Hong et al. *Anal. Chem.* **2014**	pool	+	+	20	USA	term	35	24
31	Olivares et al. *Eur. J. Nutr.* **2014**	**Sec/NS**	+	+	24	Europe	term	30	8
32	Sakaguchi et al. *Rapid Commun. M. S.* **2014**	n. a.	+		1	Japan	term	10, 90	6
33	Van Niekerk et al. *J. Nutr.* **2014**	**Sec/NS**	+	+	82	South Africa	*preterm*	4, 28	15
34	Spevacek at al. *J. Nutr.* **2015**	pool	+	+	25	USA	term & *preterm*	0-5, 14, 28	12
35	Monti et al. *J. Chromatogr. A* **2015**	n. a.	+	+	2	Italy	term	n. a.	3
36	Austin et al. *Nutrients* **2016**	pool	+	+	446	China	term	5-11, 12-30, 1-2m, 2-4m, 4-8m	10
37	Kunz et al. *JPGN* **2017**	**Sec/NS**	+	+	32	Spain	term	1-7, 8-15, >16	16
38	Sprenger et al. *PlosOne* **2017**	**Sec/NS**	+	+	50	Singapore	term	1m, 2m, 4m	5
39	McGuire et al. *Am. J. Clin. Nutr.* **2017**	**Sec/NS**	+	+	410	Afrika, Europe, NAm, SAm	term	2w to 5m	19

Abbreviations: Sec **=** Secretor (milk group 1 and 3 are secretors); NS = Non-secretor (milk group 2 and 4 are non-secretors); m = months; w = weeks; NAm = North America; SAm = South America.

Summary of all reported data for 2'-FL and LNnT

#	Reference	No of Samples	Population	Term/ Preterm	Lactation phase (days)	Milk group	Secretor status	Other discriminator	LNnT (g/L)	2'FL (g/L)
2	Thurl et al. Anal. Biochem. 1996	1	Europe	term	mature milk	1	Secretor	n.a.	0,110	1,840
3	Chaturvedi et al. Anal. Biochem. 1997	50	Latin America	term	30-60	pool	pool	n.a.	0,180	1,210
4	Coppa et al. Acta Paediatr. Suppl. 1999	18	Europe	term	4	1	Secretor	n.a.	2,040	3,930
					10				1,830	3,020
					30				1,400	2,780
					60				0,950	1,840
					90				1,370	2,460
5	Nahkla et al. Br. J. Nutr. 1999	13	US	preterm	0-33	pool	pool	n.a.	0,081	1,134
		2		term	4-128				0,048	1,273
7	Erney et al. JPGN 2000	11	Asia	term	0-2	pool	pool	n.a.	0,380	2,290
		25			3-10				0,360	2,260
		20			11-30				0,230	2,360
		24			>31				0,100	1,500
		8	Europe	term	0-2	pool	pool	n.a.	0,440	3,400
		14			3-10				0,550	2,690
		21			11-30				0,280	2,380
		25			>31				0,200	2,360
		19	Latin America	term	3-10	pool	pool	n.a.	0,410	2,790
		129			11-30				0,310	2,610
		49			>31				0,190	1,910
		4	US	term	3-10	pool	pool	n.a.	0,360	2,780
		8			11-30				0,200	2,560
		24			>31				0,190	1,690
9	Erney et al, Bioactive Comp. Hum. Milk 2001	268	America & Europe	term	1-100	pool	pool	n.a.	0,270	2,380
10	Chaturvedi et al. Glycobiol. 2001	12	US	term	mature milk	pool	pool	n.a.	0,170	2,430
11	Sumiyoshi et al. Br. J. Nutr. 2003	16	Japan	term	4	pool	pool	n.a.	0,211	n.a.
					10				0,209	
					30				0,156	
					100				0,044	
13	Morrow et al, J. Pediatr. 2004	93	Latin America	term	1-100	pool	pool	n.a.	n.a.	3,850
14	Musumeci et al. JPGN 2006	53	Africa	term	1	pool	pool	n.a.	n.a.	1,800
					2					4,500
					3					8,400
		50	Europe	term	1	pool	pool	n.a.	n.a.	1,000
					2					2,100
					3					4,200
17	Asakuma et al. Eur. J. Clin. Nutr. 2008	12	Japan	term	1-3	pool	pool	n.a.	0,460	2,026
18	Leo et al. J. Chromatogr. 2009	8	Samoa	term	5-10	pool	poo	n.a.	0,460	0,220
					> 10				0,200	0,690
19	Thurl et al. Br. J. Nutr. 2010	21	Germany	term	3	1	Secretor	n.a.	0,490	4,130
		109			3-90				0,320	3,130
		28			3-90	2	Non-secretor	n.a.	0,110	0,000
		17			3-90	3	Secretor	n.a.	0,320	4,570
20	Leo et al. Biosci. Biotech. Biochem. 2010	16	Samoa	term	5-10	pool	pool	n.a.	0,460	0,220
					22-155				0,200	0,690
21	Asakuma et al. J. Biol. Chem. 2011	57	Japan	term	30-120	pool	pool	n.a.	0,320	1,480
22	Coppa et al. JPGN 2011	10	Europe	term	25-35	1	Secretor	n.a.	n.a.	2,560
		19				2	Non-secretor			0,000
		6				3	Secretor			2,660
		4				4	Non-secretor			0,000

#	Reference	No of Samples	Population	Term/ Preterm	Lactation phase (days)	Milk group	Secretor status	Other discriminator	LNnT (g/L)	2'FL (g/L)
23	Gabrielli et al. Pediatr. 2011	35	Europe	preterm	4	1	Secretor	n.a.	1,970	7,230
					10				1,660	5,360
					20				1,640	4,720
					30				1,610	4,410
		18			4	2	Non-secretor	n.a.	1,440	0,000
					10				1,850	0,000
					20				1,750	0,000
					30				1,290	0,000
		7			4	3	Secretor	n.a.	1,200	7,360
					10				1,630	6,690
					20				1,150	5,830
					30				1,360	5,850
		3			4	4	Non-secretor	n.a.	1,250	0,000
					10				1,400	0,000
					20				1,770	0,000
					30				1,000	0,000
24	Galeotti et al. Anal. Biochem. 2012	n/a	Europe	term	4-30	1	Secretor	Method A	1,850	3,710
								Method B	1,755	4,110
						2	Non-secretor	Method A	2,940	0,000
								Method B	3,080	0,000
						3	Secretor	Method A	2,565	6,570
								Method B	2,420	7,150
						4	Non-secretor	Method A	2,236	0,000
								Method B	3,525	0,000
27	Bao et al. Anal. Biochem. 2013	4	US	term	3	1	Secretor	n.a.	0,231	1,117
					14-29				0,629	1,078
28	Smilowitz et al. J. Nutr. 2013	52	US	term	90	pool	pool	n.a.	0,090	1,220
29	Galeotti et al. Electrophoresis 2014	3	Europe	term	4-30	1	Secretor	n.a.	4,100	5,000
		3				2	Non-secretor		3,300	0,000
		2				3	Secretor		0,000	7,800
		1				4	Non-secretor		2,500	0,000
30	Hong et al. Anal. Chem. 2014	20	USA	term	35	1+3	Secretor	n.a.	0,360	2,500
						2+4	Non-secretor		0,220	0,480
31	Olivares et al. Eur. J. Nutr. 2014	24	Europe	term	30	1+3	Secretor	Celiac+	n.a.	2,540
								Celiac–		2,510
						2+4	Non-secretor	Celiac+		0,080
								Celiac–		0,070
33	Van Niekerk et al. J. Nutr. 2015	82	South Africa	pre-term	4	1+3	Secretor	HIV–	0,192	1,227
								HIV+	0,154	0,697
					28			HIV–	0,200	0,680
								HIV+	0,160	0,520
					4	2+4	Non-secretor	HIV–	0,269	0,010
								HIV+	0,272	0,010
					28			HIV–	0,200	0,010
								HIV+	0,280	0,010
34	Spevacek at al. J. Nutr. 2015	15	USA	term	0-5	pool	pool	n.a.	0,260	2,650
					14				0,150	2,060
					28				0,120	1,750
		10		pre-term	0-5				0,160	2,420
					14				0,120	1,660
					28				0,150	1,130

#	Reference	No of Samples	Population	Term/ Preterm	Lactation phase (days)	Milk group	Secretor status	Other discriminator	LNnT (g/L)	2'FL (g/L)
36	Austin et al. Nutrients 2016	446	China	term	5-11	pool	pool	n.a.	0,180	2,600
					12-30				0,120	2,300
					1-2 months				0,085	2,200
					2-4 months				0,065	1,800
					4-8 months				0,059	1,300
37	Kunz et al. JPGN 2016	32	Spain	term	1-7	1+3	Secretor	n.a.	0,290	3,990
					8-15				0,240	3,600
					> 16				0,190	2,760
					1-7	2	Non-secretor		0,250	0,000
					8-15				0,170	0,000
					> 16				0,170	0,000
38	Sprenger et al. PlosOne 2017	34	Singapore	term	1 month	1+3	Secretor	n.a.	0,263	2,170
					2 months				0,166	1,764
					4 months				0,108	1,376
		16			1 month	2+4	Non-secretor		0,189	0,026
					2 months				0,109	0,019
					4 months				0,066	0,011
39	McGuire et al. Am. J. Clin. Nutr. 2017	40	Ethiopia	term	2 weeks to 5 months	pool	pool	*rural*	0,593	1,105
		40						*urban*	0,656	1,393
		80						*pool*	0,625	1,249
		40				1+3	Secretor	*rural*	0,554	1,701
		40						*urban*	0,616	1,798
		80						*pool*	0,585	1,750
		40				2+4	Non-secretor	*rural*	0,666	0,002
		40						*urban*	0,793	0,000
		80						*pool*	0,730	0,001
		40	Gambia	term	2 weeks to 5 months	pool	pool	*rural*	1,008	1,440
		40				pool		*urban*	0,553	2,061
		80				pool		*pool*	0,781	1,751
		40				1+3	Secretor	*rural*	0,822	2,216
		40				1+3		*urban*	0,533	2,425
		80				1+3		*pool*	0,678	2,321
		40				2+4	Non-secretor	*rural*	1,351	0,001
		40				2+4		*urban*	0,668	0,001
		80				2+4		*pool*	1,010	0,001
		40	Ghana	term	2 weeks to 5 months	pool	pool	n.a.	0,613	0,702
						1+3	Secretor		0,583	1,036
						2+4	Non-secretor		0,675	0,010
		42	Kenya	term	2 weeks to 5 months	pool	pool	n.a.	0,759	1,651
						1+3	Secretor		0,699	2,039
						2+4	Non-secretor		1,016	0,001
		43	Peru	term	2 weeks to 5 months	pool	pool	n.a.	0,416	3,188
						1+3	Secretor		0,391	3,264
						2+4	Non-secretor		1,474	0,001
		41	Spain	term	2 weeks to 5 months	pool	pool	n.a.	0,388	1,907
						1+3	Secretor		0,364	2,523
						2+4	Non-secretor		0,461	0,001
		24	Sweden	term	2 weeks to 5 months	pool	pool	n.a.	0,604	2,765
						1+3	Secretor		0,600	3,490
						2+4	Non-secretor		0,618	0,010
		41	USA	term	2 weeks to 5 months	pool	pool	WA state	0,549	2,031
						1+3	Secretor		0,562	2,974
						2+4	Non-secretor		0,624	0,003
		19				pool	pool	CA state	0,561	3,440
						1+3	Secretor		0,514	3,631
						2+4	Non-secretor		0,541	0,001

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