

ESM Table 1 – The risk of islet autoimmunity (IA) and type 1 diabetes associated with weight and length/height z-scores by age and time-varying model of growth up to 10 years of age in children having first-degree relative/s with type 1 diabetes and increased HLA-conferred risk of type 1 diabetes (N=2,149)

| | Any IA ^a (n=305) | | | IAA First Antibody (n=183) | | | GADA First Antibody (n=189) | | | Multiple IA* (n=190) | | |
|--|--------------------------------|-----------|---------|-------------------------------|-----------|---------|--------------------------------|-----------|---------|-------------------------|-----------|---------|
| Age, years | HR | 95% CI | P value | HR | 95% CI | P value | HR | 95% CI | P value | HR | 95% CI | P value |
| Weight z score | | | | | | | | | | | | |
| 1 | 1.12 | 0.99-1.26 | 0.07 | 1.10 | 0.94-1.28 | 0.25 | 0.97 | 0.84-1.13 | 0.74 | 1.11 | 0.95-1.30 | 0.18 |
| 2 | 1.05 | 0.93-1.19 | 0.42 | 1.08 | 0.93-1.27 | 0.32 | 1.00 | 0.86-1.16 | 0.98 | 1.14 | 0.97-1.34 | 0.11 |
| 3 | 1.05 | 0.92-1.20 | 0.48 | 1.11 | 0.94-1.31 | 0.24 | 0.98 | 0.83-1.14 | 0.76 | 1.16 | 0.97-1.39 | 0.09 |
| 4 | 1.07 | 0.92-1.23 | 0.39 | 1.05 | 0.88-1.25 | 0.59 | 0.98 | 0.83-1.16 | 0.80 | 1.16 | 0.96-1.41 | 0.12 |
| 5 | 1.06 | 0.91-1.23 | 0.45 | 1.02 | 0.85-1.22 | 0.87 | 1.02 | 0.87-1.20 | 0.79 | 1.21 | 0.99-1.48 | 0.06 |
| 6 | 1.07 | 0.93-1.23 | 0.37 | 1.01 | 0.85-1.20 | 0.95 | 1.06 | 0.90-1.24 | 0.50 | 1.24 | 1.02-1.51 | 0.03 |
| 7 | 1.05 | 0.91-1.21 | 0.52 | 1.02 | 0.85-1.21 | 0.86 | 0.98 | 0.84-1.15 | 0.80 | 1.17 | 0.96-1.43 | 0.13 |
| 8 | 1.03 | 0.89-1.20 | 0.64 | 1.03 | 0.87-1.23 | 0.73 | 1.05 | 0.90-1.24 | 0.53 | 1.07 | 0.87-1.31 | 0.53 |
| 9 | 1.03 | 0.88-1.20 | 0.71 | 1.03 | 0.86-1.24 | 0.75 | 1.03 | 0.87-1.22 | 0.73 | 1.14 | 0.91-1.43 | 0.26 |
| 10 | 0.96 | 0.82-1.13 | 0.62 | 1.07 | 0.89-1.28 | 0.48 | 0.99 | 0.84-1.17 | 0.93 | 0.98 | 0.76-1.26 | 0.87 |
| Length/height z score | | | | | | | | | | | | |
| 1 | 1.08 | 0.95-1.23 | 0.25 | 1.10 | 0.93-1.31 | 0.26 | 0.98 | 0.83-1.16 | 0.86 | 1.08 | 0.91-1.27 | 0.40 |
| 2 | 1.03 | 0.90-1.18 | 0.66 | 0.95 | 0.80-1.13 | 0.55 | 1.01 | 0.86-1.19 | 0.88 | 1.16 | 0.97-1.38 | 0.10 |
| 3 | 1.08 | 0.94-1.24 | 0.29 | 1.03 | 0.87-1.22 | 0.75 | 1.00 | 0.85-1.18 | 1.00 | 1.21 | 1.01-1.45 | 0.04 |
| 4 | 1.03 | 0.89-1.18 | 0.72 | 1.01 | 0.84-1.20 | 0.95 | 1.00 | 0.85-1.18 | 0.99 | 1.08 | 0.90-1.30 | 0.42 |
| 5 | 1.05 | 0.91-1.21 | 0.54 | 1.02 | 0.85-1.22 | 0.81 | 1.02 | 0.87-1.20 | 0.82 | 1.14 | 0.94-1.39 | 0.18 |
| 6 | 0.96 | 0.84-1.10 | 0.56 | 0.96 | 0.81-1.14 | 0.63 | 1.00 | 0.85-1.17 | 0.97 | 1.01 | 0.83-1.22 | 0.91 |
| 7 | 0.96 | 0.83-1.11 | 0.58 | 0.94 | 0.78-1.13 | 0.52 | 0.96 | 0.81-1.13 | 0.60 | 1.03 | 0.84-1.26 | 0.79 |
| 8 | 1.00 | 0.87-1.16 | 0.96 | 1.00 | 0.84-1.20 | 0.98 | 1.00 | 0.85-1.19 | 0.96 | 1.04 | 0.85-1.28 | 0.71 |
| 9 | 1.00 | 0.86-1.17 | 0.96 | 1.01 | 0.83-1.22 | 0.93 | 0.97 | 0.81-1.15 | 0.69 | 1.04 | 0.83-1.30 | 0.75 |
| 10 | 0.96 | 0.82-1.14 | 0.67 | 1.06 | 0.88-1.29 | 0.53 | 0.95 | 0.80-1.13 | 0.59 | 0.93 | 0.72-1.20 | 0.58 |
| Weight z score up to 10 years | 1.10 | 0.97-1.25 | 0.13 | 1.10 | 0.93-1.29 | 0.28 | 1.02 | 0.87-1.19 | 0.80 | 1.19 | 1.02-1.39 | 0.03 |
| Length/height z score up to 10 years | 1.08 | 0.95-1.22 | 0.27 | 0.93 | 0.78-1.11 | 0.42 | 0.98 | 0.84-1.16 | 0.85 | 1.22 | 1.03-1.43 | 0.02 |
| Weight z score (joint modeling) | 1.06 | 0.91-1.23 | 0.43 | 1.01 | 0.83-1.22 | 0.96 | 0.98 | 0.81-1.17 | 0.79 | 1.16 | 0.96-1.40 | 0.13 |
| Length/height z score (joint modeling) | 1.09 | 0.93-1.27 | 0.29 | 1.01 | 0.83-1.23 | 0.93 | 1.02 | 0.84-1.24 | 0.82 | 1.19 | 0.98-1.45 | 0.08 |

^aAntibodies include insulin autoantibodies (IAA), islet antigen-2, GAD (GADA), and zinc transporter 8 autoantibodies.

HRs adjusted for birth weight z score (for weight z-score models) and birth length z-score (for length/height z-score models), sex, HLA risk, maternal type 1 diabetes status, mode of delivery, and breastfeeding duration and stratified by region of residence. Presented p-values are nominal (uncorrected) p-values, and were considered significant if < 0.005.

ESM Table 2 – The risk of islet autoimmunity (IA) associated with overweight (includes obese) and obesity by age and time-varying model of overweight (includes obese) and obesity and up to 10 years of age using International Obesity Task Force BMI cut-off points (N=2,149)

| | Any IA ^a (n=305) | | | IAA First Antibody (n=183) | | | GADA First Antibody (n=189) | | | Multiple IA * (n=190) | | |
|-----------------------------|--------------------------------|-----------|---------|-------------------------------|-----------|---------|--------------------------------|-----------|---------|--------------------------|-----------|---------|
| Age, years | HR | 95% CI | P value | HR | 95% CI | P value | HR | 95% CI | P value | HR | 95% CI | P value |
| Overweight (%) | | | | | | | | | | | | |
| 2 | 0.92 | 0.59-1.44 | 0.73 | 0.90 | 0.51-1.60 | 0.73 | 0.90 | 0.53-1.53 | 0.69 | 0.93 | 0.52-1.65 | 0.80 |
| 3 | 0.84 | 0.56-1.25 | 0.39 | 1.00 | 0.62-1.61 | 0.99 | 1.04 | 0.66-1.63 | 0.86 | 0.76 | 0.44-1.31 | 0.32 |
| 4 | 1.22 | 0.86-1.73 | 0.27 | 0.96 | 0.59-1.55 | 0.85 | 1.11 | 0.72-1.70 | 0.64 | 1.28 | 0.81-2.03 | 0.30 |
| 5 | 1.02 | 0.71-1.47 | 0.90 | 1.03 | 0.65-1.62 | 0.90 | 1.16 | 0.79-1.72 | 0.44 | 1.45 | 0.92-2.28 | 0.11 |
| 6 | 1.15 | 0.80-1.64 | 0.45 | 1.12 | 0.72-1.74 | 0.62 | 1.12 | 0.76-1.67 | 0.56 | 1.54 | 0.96-2.45 | 0.07 |
| 7 | 1.01 | 0.72-1.43 | 0.95 | 1.12 | 0.74-1.70 | 0.60 | 1.00 | 0.68-1.45 | 0.98 | 1.31 | 0.83-2.06 | 0.25 |
| 8 | 0.94 | 0.66-1.32 | 0.71 | 1.23 | 0.83-1.82 | 0.31 | 1.01 | 0.69-1.47 | 0.96 | 1.13 | 0.71-1.79 | 0.62 |
| 9 | 0.92 | 0.65-1.31 | 0.64 | 1.37 | 0.93-2.02 | 0.11 | 0.90 | 0.61-1.32 | 0.59 | 1.11 | 0.67-1.82 | 0.68 |
| 10 | 0.75 | 0.51-1.11 | 0.15 | 1.12 | 0.74-1.70 | 0.60 | 0.98 | 0.67-1.44 | 0.93 | 0.85 | 0.47-1.53 | 0.59 |
| Obesity (%) | | | | | | | | | | | | |
| 2 | 1.24 | 0.50-3.03 | 0.64 | 0.89 | 0.22-3.61 | 0.87 | 1.45 | 0.53-3.95 | 0.47 | 1.67 | 0.61-4.61 | 0.32 |
| 3 | 0.97 | 0.40-2.36 | 0.94 | 1.64 | 0.67-4.04 | 0.28 | 1.37 | 0.56-3.37 | 0.49 | 1.01 | 0.32-3.20 | 0.99 |
| 4 | 1.68 | 0.88-3.21 | 0.12 | 1.76 | 0.81-3.81 | 0.15 | 1.16 | 0.51-2.65 | 0.72 | 2.18 | 1.00-4.76 | 0.05 |
| 5 | 1.20 | 0.66-2.18 | 0.55 | 0.94 | 0.41-2.15 | 0.88 | 0.90 | 0.43-1.85 | 0.77 | 1.56 | 0.75-3.26 | 0.24 |
| 6 | 1.27 | 0.74-2.18 | 0.38 | 0.96 | 0.47-1.99 | 0.92 | 1.05 | 0.56-1.95 | 0.89 | 1.58 | 0.78-3.17 | 0.20 |
| 7 | 1.33 | 0.80-2.22 | 0.27 | 1.42 | 0.77-2.63 | 0.26 | 1.15 | 0.66-2.02 | 0.62 | 1.25 | 0.60-2.63 | 0.55 |
| 8 | 1.20 | 0.73-1.97 | 0.48 | 1.67 | 0.97-2.88 | 0.06 | 1.31 | 0.78-2.21 | 0.31 | 1.38 | 0.71-2.70 | 0.35 |
| 9 | 1.26 | 0.75-2.12 | 0.38 | 1.26 | 0.68-2.34 | 0.46 | 1.11 | 0.63-1.97 | 0.71 | 1.35 | 0.64-2.87 | 0.43 |
| 10 | 0.99 | 0.55-1.78 | 0.98 | 1.37 | 0.75-2.50 | 0.30 | 1.11 | 0.63-1.97 | 0.71 | 0.96 | 0.38-2.46 | 0.94 |
| Overweight up to 10 years | 0.99 | 0.65-1.49 | 0.94 | 1.08 | 0.62-1.88 | 0.80 | 0.76 | 0.46-1.26 | 0.28 | 1.21 | 0.74-1.98 | 0.45 |
| Obesity up to 10 years | 0.67 | 0.27-1.64 | 0.38 | 1.28 | 0.51-3.21 | 0.60 | 0.55 | 0.20-1.52 | 0.25 | 1.96 | 0.94-4.12 | 0.07 |
| Overweight (joint modeling) | 0.68 | 0.41-1.12 | 0.13 | 0.63 | 0.32-1.22 | 0.17 | 0.81 | 0.45-1.44 | 0.47 | 1.15 | 0.63-2.10 | 0.65 |
| Obesity (joint modeling) | | | | | | | | | | | | |

^aAntibodies include insulin autoantibodies (IAA), islet antigen-2, GAD (GADA), and zinc transporter 8 autoantibodies.

BMI – body mass index.

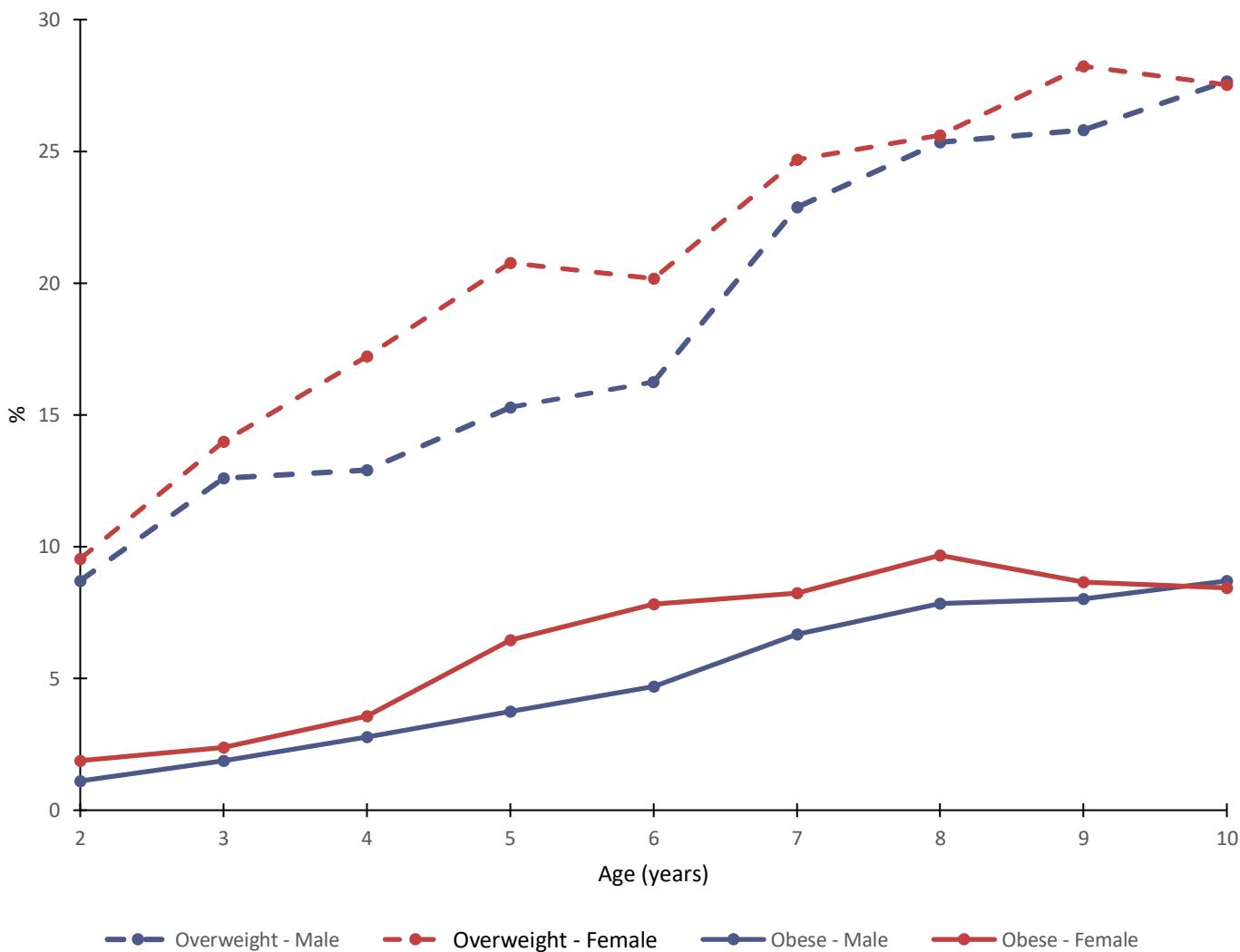
HRs adjusted for birth weight z score and birth length z score, sex, HLA risk, maternal type 1 diabetes status, mode of delivery, and breastfeeding duration and stratified by region of residence. Presented p-values are nominal (uncorrected) p-values, and were considered significant if < 0.005. Shaded analyses: model failed to converge.

ESM Table 3 – The risk of type 1 diabetes associated with weight and length/height z-scores by age and time-varying model of growth up to 10 years of age in children having first-degree relative/s with type 1 diabetes and increased HLA-conferred risk of type 1 diabetes (N=2,149)

| | From multiple IA ^a to Type 1 Diabetes (n=133) | | | Type 1 Diabetes (n=172) | | |
|--|---|-----------|---------|-------------------------|-----------|---------|
| Age, years | HR | 95% CI | P value | HR | 95% CI | P value |
| Weight (z score) | | | | | | |
| 1 | 1.22 | 0.97-1.53 | 0.09 | 1.22 | 1.03-1.44 | 0.02 |
| 2 | 1.34 | 1.06-1.68 | 0.01 | 1.25 | 1.05-1.49 | 0.01 |
| 3 | 1.48 | 1.13-1.92 | 0.004 | 1.27 | 1.04-1.55 | 0.02 |
| 4 | 1.33 | 1.00-1.77 | 0.05 | 1.20 | 0.96-1.51 | 0.11 |
| 5 | 1.35 | 0.99-1.83 | 0.06 | 1.23 | 0.96-1.57 | 0.10 |
| 6 | 1.57 | 1.12-2.19 | 0.009 | 1.31 | 1.02-1.69 | 0.03 |
| 7 | 1.51 | 1.08-2.10 | 0.02 | 1.16 | 0.89-1.51 | 0.27 |
| 8 | 1.42 | 1.01-1.99 | 0.04 | 1.23 | 0.93-1.62 | 0.15 |
| 9 | 1.79 | 1.10-2.90 | 0.02 | 1.36 | 0.97-1.90 | 0.07 |
| 10 | 3.69 | 1.40-9.69 | 0.008 | 1.15 | 0.76-1.73 | 0.52 |
| Length/height z score | | | | | | |
| 1 | 1.03 | 0.83-1.28 | 0.79 | 1.03 | 0.86-1.23 | 0.78 |
| 2 | 1.10 | 0.85-1.42 | 0.48 | 1.19 | 0.99-1.44 | 0.06 |
| 3 | 1.10 | 0.86-1.41 | 0.46 | 1.15 | 0.94-1.41 | 0.17 |
| 4 | 1.04 | 0.81-1.35 | 0.75 | 1.02 | 0.82-1.27 | 0.84 |
| 5 | 0.96 | 0.72-1.29 | 0.80 | 1.07 | 0.84-1.36 | 0.58 |
| 6 | 0.92 | 0.69-1.25 | 0.61 | 0.96 | 0.75-1.23 | 0.73 |
| 7 | 1.11 | 0.81-1.54 | 0.51 | 1.01 | 0.77-1.33 | 0.94 |
| 8 | 1.04 | 0.72-1.51 | 0.82 | 1.10 | 0.82-1.46 | 0.52 |
| 9 | 1.38 | 0.82-2.32 | 0.22 | 1.06 | 0.75-1.48 | 0.74 |
| 10 | 1.04 | 0.47-2.26 | 0.93 | 0.79 | 0.51-1.21 | 0.28 |
| Weight z-score up to 10 years | 1.28 | 1.03-1.60 | 0.03 | 1.30 | 1.06-1.60 | 0.01 |
| Length/height z score up to 10 years | 1.08 | 0.86-1.35 | 0.51 | 1.27 | 1.03-1.58 | 0.03 |
| Weight z score (joint modeling) | 1.53 | 1.16-2.03 | 0.003 | 1.43 | 1.20-1.72 | <0.001 |
| Length/height z score (joint modeling) | 1.32 | 0.98-1.78 | 0.07 | 1.20 | 0.98-1.45 | 0.07 |

^aAntibodies include insulin autoantibodies, islet antigen-2, GAD, and zinc transporter 8 autoantibodies; the number of children with multiple IA = 190.
IA – islet autoimmunity.

HRs adjusted for birth weight z score and birth length z score, sex, HLA risk, maternal type 1 diabetes status, mode of delivery, and breastfeeding duration and stratified by region of residence. Presented p-values are nominal (uncorrected) p-values, and were considered significant if < 0.005.



ESM Fig 1 – Proportion (%) of overweight (including obese) and obese children aged 2 to 10 years

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| | SPA02 - Madrid - Hospital Clinico San Carlos | Serrano-Ríos Martínez-Larrad Hawkins | Manuel María Teresa Federico Gustavo | National Investigator Local Coordinator Co-Investigator |
| | SPA03 - Madrid - Hospital Gregorio Marañon | Rodriguez Arnau | Dolores | Co-Investigator |
| Sweden | SWE01 - Linköping - University of Linköping | Ludvigsson Smolinska Konefal | Johnny Malgorzata | National Investigator National Coordinator |
| | SWE02 - Uddevalla - Uddevalla Hospital | Hanas | Ragnar | Local Investigator |

| | | | | |
|--------------------|--|--------------------------------|----------------------------|---|
| | SWE03 - Göteborg - GothenburgThe Queen Silvia Children's Hospital | Lindblad | Bengt | Local Investigator |
| | SWE05 - Halmstad - Halmstad Hospital | Nilsson | Nils-Östen | Local Investigator |
| | SWE06 - Trollhättan - Trollhättan Hospital | Fors | Hans | Local Investigator |
| | SWE07 - Norrköping - Vrinnevi Hospital | Nordwall | Maria | Local Investigator |
| | SWE08 - Borås - Borås Hospital | Lindh | Agne | Local Investigator |
| | SWE09 - Karskrona - Karlskrona Hospital | Edenwall | Hans | Local Investigator |
| | SWE10 - Örebro - University Hospital | Åman | Jan | Local Investigator |
| | SWE11 - Jönköping - Ryhovs Hospital | Johansson | Calle | Local Investigator |
| Switzerland | SWT01 - Zürich - University Children's Hospital | Gradient Konrad Schoenle | Margrit Daniel Eugen | Local Coordinator National Investigator National Investigator |
| USA | USA01 - Pittsburgh - Children's Hospital of Pittsburgh | Becker | Dorothy | USA National Investigator / Pittsburgh Local Investigator |
| | | Daftary Klein | Ashi Mary Beth | Co-Investigator Pittsburgh Coordinator |
| | | Gilmour | Carol | Co-Investigator |
| | USA02 - Seattle - VA Puget Sound Health Care | Palmer Malone | Jerry Patty | Local Investigator Coordinator |

| System and University of Washington | | | | |
|---|--|-----------------------------------|---|--|
| USA03 - St. Louis - Washington University | Tanner-Blasiar White | Marilyn Neil | Coordinator Local Investigator | |
| USA04 - Los Angeles - Mattel Children's Hospital of UCLA | Devaskar Horowitz Rogers | Uday Heather Lisa | Local Investigator Coordinator/dietitian Coordinator/dietitian | |
| USA05 - Ponce - Ponce School of Medicine | Colon Frazer Torres | Roxana Teresa Jose | Coordinator Co-Investigator Local Investigator | |
| USA06 - New York - Naomie Berrie Diabetes Center | Goland Greenberg Schachner Softness | Robin Ellen Holly Barney | Local Investigator Coordinator Co-Investigator Co-Investigator | |
| Laboratories | HLA-typing Laboratory - Turku - Finland | Ilonen | Jorma | Head of HLA-typing Laboratory |
| | HLA-typing Laboratory - Pittsburgh - PA - USA | Trucco | Massimo | Head of HLA-typing Laboratory |
| | | Nichol | Lynn | Chief Technician |
| | Cow's Milk Antibody Laboratory - Helsinki - Finland | Savilahti | Erkki | Head of Cow's Milk Antibody Laboratory |
| | Autoantibody Laboratory - Helsinki – Finland | Härkönen Knip | Taina Mikael | Co-Investigator Head of Antibody Laboratory |
| T-Cell Laboratory - Helsinki – Finland | | Vaarala Luopajarvi | Outi Kristiina | Head of T-cell Laboratory Co-Investigator |

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