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| **Supplementary file 1A. Characteristics of participants of the 1st and 2nd study.** |
|  | Study 1 (CUMC 1) | Study 2 (INSERM) |
| Number  | 11 | 9 |
| Gender  | Females | Females |
| Age (years) | 27.9 ± 0.7 | 26.1 ± 1.0 |
| BMI (kg/m2) | 21.8 ± 0.6 | 20.8 ± 0.5 |
| Fasting glucose (mg/dL) | 79.9 ± 1.3 | - |
| Fasting LCN2 (ng/mL) | 38.5 ± 7.6 | 74.4 ± 8.8 |
| Peak LCN2 (ng/mL) | 44.6 ± 7.8 (‡) | 114.6 ± 16.5 (\*) |
| Change from baseline | 16% | 54% |
| Fasting GLP-1 (ng/mL) | 51.9 ± 3.5 | 11.9 ± 2.0 |
| Peak GLP-1 (ng/mL) | 85.5 ± 5.5 (\*) | 18.0 ± 2.0 (\*) |
| Change from baseline | 65% | 90% |
| Major GLP-1 change at (min) | 45 | 60 |
| Major LCN2 change at (min) | 45 | 60 |
| Fasting insulin (mIU/mL) | 1.6 ± 0.3 | 8.9 ± 1.9 |
| Peak insulin (mIU/mL) | 9.2 ± 2.6 (\*) | 65.4 ± 16.4 (\*) |
| Change from baseline | 473% | 659% |
| Major insulin change at (min) | 30 | 60 |
| Contains raw (i.e. non-transformed data) based on which % change of postprandial concentrations was calculated. Values represent mean ± SEM. \* indicates P<0.05 and ‡ indicates P<0.06 versus fasting state for each protein with two-tailed Student’s t-, Wilcoxon or Mann Whitney tests. *BMI = Body Mass Index, GLP-1 = Glucagon-like peptide 1, LCN2 = Lipocalin-2, IU=International Units.* |

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| **Supplementary file 1B. Characteristics of study participants of the 3rd study.** |
|  | *Study 3**(Rutgers)* |
| *Number*  | 47 (R:25, NR 22) | 28 (R: 15, NR: 13) | 19 (R: 10, NR:9) |
| *Gender*  | Mixed | Females | Males |
| *Age (years)* | R: 32.1 ± 2.4 NR: 32.8 ± 2.6 | R: 36.4 ± 3.5 NR: 35.6 ± 3.9 | R: 25.7 ± 2.0 NR: 28.7 ± 2.7 |
| *BMI (kg/m2)* | R: 28.2 ± 0.6NR: 29.2 ± 0.7 | R: 27.9 ± 0.7NR: 30.0 ± 1.1 | R: 28.7 ± 1.3NR: 28.1 ± 0.9 |
| *% Body Fat* | R: 26.4 ± 1.4NR: 28.2 ± 1.4 | R: 29.4 ± 1.7NR: 32.1 ± 1.6 | R: 22.1 ± 2.0NR: 22.6 ± 1.8 |
| *WC (cm)* | R: 94.6 ± 2.0NR: 102.4 ± 3.4(†) | R: 92.3 ± 2.5NR: 104.0 ± 5.4(\*) | R: 98.2 ± 3.7NR: 100.1 ± 4.9 |
| *SBP (mm Hg)* | R: 110.0 ± 2.8NR: 107.9 ± 3.5 | R: 110.9 ± 3.7NR: 105.0 ± 3.5 | R: 108.6 ± 5.2NR: 112.0 ± 7.9 |
| *DBP (mm Hg)* | R: 81.8 ± 2.0NR: 83.6 ± 2.4 | R: 79.1 ± 2.1NR: 83.3 ± 3.8 | R: 86.0 ± 4.1NR: 84.0 ± 3.1 |
| *Fasting Glucose (mg/dL)* | R: 92.2 ± 1.4NR: 94.5 ± 1.9 | R: 93.5 ± 1.9NR: 95.6 ± 3.2 | R: 90.3 ± 2.4NR: 92.8 ± 2.4 |
| *Fasting Lipocalin-2 (ng/mL)* | R: 34.7 ± 4.1NR: 37.6 ± 2.8(†) | R: 33.0 ± 3.6NR: 39.4 ± 4.2 | R: 37.1 ± 8.9NR: 35.1 ± 3.1 |
| *Peak Lipocalin-2 (ng/mL)* | R: 38.8 ± 4.9NR: 30.5 ± 2.2 | R: 36.3 ± 4.2NR: 30.7 ± 3.5 | R: 42.7 ± 10.4NR: 29.7 ± 3.0 |
| *Change from baseline* | R: +12%NR: -19% | R: +10% NR: -22% | R: +15%NR: -16% |
| *Major LCN2 change at (min)* | R: 60NR: 60 | R: 60NR: 60 | R: 60 NR: 90  |
| *Fasting GLP-1 (ng/mL)* | R: 81.3 ± 6.1NR: 75.1 ± 7.1 | R: 73.8 ± 7.4NR: 69.0 ± 8.6 | R: 93.3 ± 9.9NR: 81.7 ± 11.6 |
| *Peak GLP-1 (ng/mL)* | R: 115.0 ± 7.1NR: 97.0 ± 7.6 | R: 113.0 ± 8.5NR: 104.2 ± 13.2 | R: 114.7 ± 12.3NR: 96.3 ± 11.6 |
| *Change from baseline* | R: +41%NR:+29% | R: +53%NR: +51% | R: +23%NR: +18% |
| *Major GLP-1 change at (min)* | R: 90NR: 120 | R: 90NR: 90 | R: 90NR: 120 |
| *Fasting insulin (mIU/mL)* | R: 17.2 ± 1.3NR: 15.9 ± 1.4 | R: 17.9 ± 2.0NR: 16.3 ± 2.0 | R: 16.1 ± 1.4NR: 15.3 ± 2.1 |
| *Peak insulin (mIU/mL)* | R: 81.7 ± 7.5NR: 96.1 ± 14.6 | R: 86.6 ± 10.8NR: 107.2 ± 16.1 | R: 74.4 ± 9.9NR: 83.9 ± 25.5 |
| *Change from baseline* | R: +375%NR:+505% | R: +384%NR: +556% | R: +362%NR: +447% |
| *Major insulin change at (min)* | R: 30NR: 30 | R: 30NR: 30 | R: 30NR: 30 |
| Contains raw (i.e. non-transformed data) based on which % change of postprandial concentration from baseline was calculated. Values represent mean ± SEM. \* indicates P<0.05, and † indicates p<0.1 of R versus NR in each cohort with two-tailed unpaired Student’s t- or Mann-Whitney tests*. R = responders (elevated LCN2 levels in multiple timepoints after the meal), NR = non-responders (reduced LCN2 levels after the meal challenge), BMI = Body Mass Index, WC = waist circumference, SBP = systolic blood pressure, DBP = diastolic blood pressure, LCN2 = Lipocalin-2, GLP-1 = Glucagon-like peptide 1, IU=international units.* |

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| **Supplementary file 1C. Characteristics of participants of the 4th study.** |
|  | *Study 4**(CUMC 2)* |
|  | Pre-RYGB | Post-RYGB |
| *Number of subjects* | 12 | 12 |
| *Gender of subjects* | 11 Females – 1 Male | 11 Females – 1 Male |
| *Age (years)* | 35.3 ± 3.0 | 36.4 ± 3.0 |
| *weight (kg)* | 128.9 ± 6.5 | 80.4 ± 5.2 (\*) |
| *BMI (kg/m2)* | 47.4 ± 1.9 | 29.6 ± 1.8 (\*) |
| *Fasting Glucose (mg/dL)* | 98.2 ± 3.8 | 86.2 ± 2.7 (\*) |
| *Fasting LCN2 (ng/mL)* | 61.4 ± 8.0 | 47.1 ± 4.8 (†) |
| *Peak LCN2 (ng/mL)* | 49.5 ± 6.6 | 75.0± 20.1 (\*) |
| *LCN2 Change from baseline* | -16% | +59% |
| *Major LCN2 change at (min)* | 90 | 90 |
| *Fasting GLP-1 (ng/mL)* | 7.4 ± 0.9 | 9.0 ± 1.3 |
| *Peak GLP-1 (ng/mL)* | 16.8 ± 2.3 | 92.2 ± 18.6 (\*) |
| *GLP-1 Change from baseline* | 140% | 1176% |
| *Major GLP-1 change at (min)* | 30 | 45 |
| *Fasting insulin (uIU/mL)* | 22.4 ± 1.9 | 5.7 ± 0.9(\*) |
| *Peak insulin (uIU/mL)* | 147.0 ± 30.7 | 267.8 ± 61.6(‡) |
| *Insulin Change from baseline* | +547% | +5935% |
| *Major insulin change at (min)* | 30 | 60 |

Contains raw (i.e. non-transformed data) based on which % change of postprandial LCN2 concentration was calculated. LCN2 Values represent mean ± SEM. \* indicates P<0.05, ‡ indicates P<0.06, † indicates P<0.1 of Post-RYGB versus Pre-RYGB with two-tailed paired Student’s t-tests or Wilcoxon tests. RYGB = Roux-en-Y Gastric Bypass, BMI = Body Mass Index, LCN2 = Lipocalin-2, GLP-1 = Glucagon-like peptide 1, IU = International Units.