Gene therapy approach for treatment of obese agouti mice

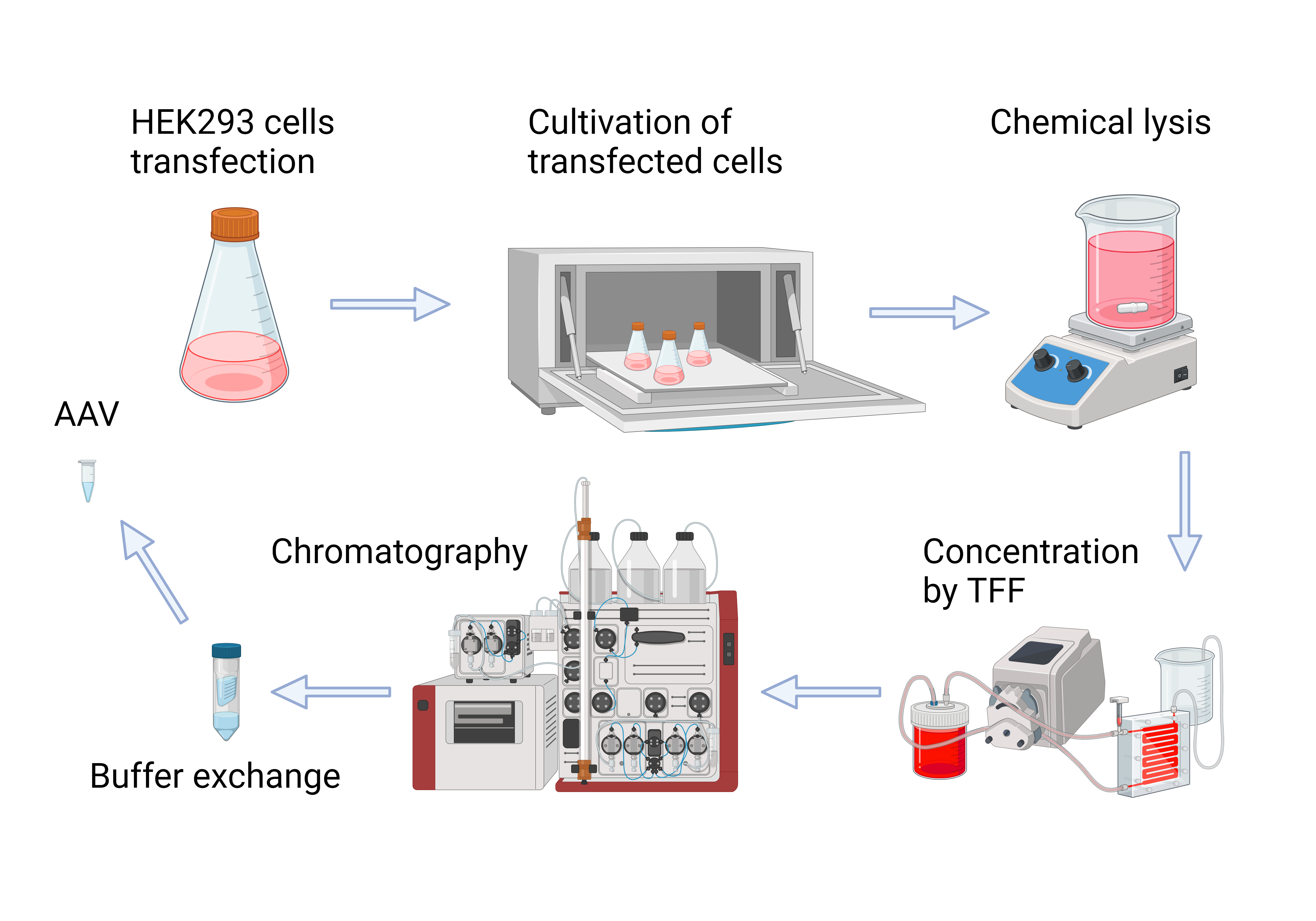
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Supplementary Data



**Figure S1**. Schematic representation of adeno-associated virus production and purification.

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**Figure S2.** Volcano plots of significantly different lipids. Lipids that pass a threshold of fold change (FC) >2.0, p value < 0.05 are highlighted by blue and red. The highlighted by red lipids were increased and the highlighted by blue decreased in mice received FoxP4-expressing AAV (A), PRDM16-expressing AAV (B) or follistatin-expressing AAV (C) compared with the control (empty AAV). Volcano plot analysis was performed in Metaboanalyst 5.0 (https://www.metaboanalyst.ca/).

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**Figure S3**. Photographic images of adipose tissue extracted from mice that were injected with empty AAV (control), AAV8-FoxP4 (FoxP4), AAV8-PRDM16 (PRDM16), and AAV9-FST (Follistatin). Scale bar: 10 mm.

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**Figure S4.** Total ion chromatogramms of iWAT lipids. Green: intra-WAT injection of empty AAV (control) and red: intra-WAT injection of AAV-FoxP4.

**Table S1.** MS/MS parameters of analyzed lipids.

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Compound** | **Polarity** | **Precursor Ion (m/z)** | **Product Ion (m/z)** | **Time segment (min)** |
| FFA C12:0 | Negative | 199.2 | 199.2 | 0-12 |
| FFA C12:1 | Negative | 197.2 | 197.2 | 0-12 |
| FFA C14:0 | Negative | 227.3 | 227.3 | 0-12 |
| FFA C14:1 | Negative | 225.2 | 225.2 | 0-12 |
| FFA C16:0 | Negative | 255.3 | 255.3 | 0-12 |
| FFA C16:1 | Negative | 253.3 | 253.3 | 0-12 |
| FFA C18:0 | Negative | 283.3 | 283.3 | 0-12 |
| FFA C18:1 | Negative | 281.3 | 281.3 | 0-12 |
| FFA C18:2 | Negative | 279.3 | 279.3 | 0-12 |
| FFA C18:3 | Negative | 277.3 | 277.3 | 0-12 |
| FFA C18:4 | Negative | 275.3 | 275.3 | 0-12 |
| FFA C20:0 | Negative | 311.3 | 311.3 | 0-12 |
| FFA C20:1 | Negative | 309.3 | 309.3 | 0-12 |
| FFA C20:3 | Negative | 305.3 | 305.3 | 0-12 |
| FFA C20:4 | Negative | 303.3 | 303.3 | 0-12 |
| FFA C20:5 | Negative | 301.3 | 301.3 | 0-12 |
| FFA C22:0 | Negative | 339.3 | 339.3 | 0-12 |
| FFA C22:1 | Negative | 337.3 | 337.3 | 0-12 |
| FFA C22:4 | Negative | 331.3 | 331.3 | 0-12 |
| FFA C22:5 | Negative | 329.3 | 329.3 | 0-12 |
| FFA C22:6 | Negative | 327.3 | 327.3 | 0-12 |
| FFA C24:0 | Negative | 367.3 | 367.3 | 0-12 |
| FFA C24:1 | Negative | 365.3 | 365.3 | 0-12 |
| FFA C24:5 | Negative | 353.3 | 353.3 | 0-12 |
| FFA C24:6 | Negative | 355.3 | 355.3 | 0-12 |
| FFA C26:0 | Negative | 395.3 | 395.3 | 0-12 |
| FFA C26:1 | Negative | 393.3 | 393.3 | 0-12 |
| FFA C28:0 | Negative | 423.4 | 423.4 | 0-12 |
| 16:0 Cholesteryl ester | Positive | 642.6 | 369.1 | 12-41 |
| 16:1 Campesteryl ester | Positive | 654.6 | 369.1 | 12-41 |
| 16:1 Cholesteryl ester | Positive | 640.6 | 369.1 | 12-41 |
| 16:2 Campesteryl ester | Positive | 652.6 | 369.1 | 12-41 |
| 16:2 Cholesteryl ester | Positive | 638.6 | 369.1 | 12-41 |
| 18:0 Cholesteryl ester | Positive | 670.6 | 369.1 | 12-41 |
| 18:1 Campesteryl ester | Positive | 682.6 | 369.1 | 12-41 |
| 18:1 Cholesteryl ester | Positive | 668.6 | 369.1 | 12-41 |
| 18:2 Cholesteryl ester | Positive | 666.6 | 369.1 | 12-41 |
| SM (d16:1/18:1) | Positive | 701.6 | 184.1 | 12-41 |
| SM (d16:1/22:1) | Positive | 757.6 | 184.1 | 12-41 |
| SM (d16:1/24:0) | Positive | 787.7 | 184.1 | 12-41 |
| SM (d16:1/24:1) | Positive | 785.6 | 184.1 | 12-41 |
| SM (d18:0/16:0) | Positive | 705.6 | 184.1 | 12-41 |
| SM (d18:0/18:0) | Positive | 733.6 | 184.1 | 12-41 |
| SM (d18:0/20:0) | Positive | 761.6 | 184.1 | 12-41 |
| SM (d18:0/22:0) | Positive | 789.7 | 184.1 | 12-41 |
| SM (d18:1/16:0) | Positive | 703.6 | 184.1 | 12-41 |
| SM (d18:1/18:0) | Positive | 731.6 | 184.1 | 12-41 |
| SM (d18:1/18:1)9Z)) | Positive | 729.6 | 184.1 | 12-41 |
| SM (d18:1/20:0) | Positive | 759.6 | 184.1 | 12-41 |
| SM (d18:1/24:0) | Positive | 815.7 | 184.1 | 12-41 |
| SM (d18:2/22:1) | Positive | 783.6 | 184.1 | 12-41 |
| SM (d18:2/24:1) | Positive | 811.7 | 184.1 | 12-41 |
| SM(24:1) | Positive | 813.7 | 184.1 | 12-41 |
| SM(26:0) | Positive | 843.7 | 184.1 | 12-41 |
| SM(26:1) | Positive | 841.7 | 184.1 | 12-41 |
| PC (30:0) | Positive | 706.5 | 184.1 | 12-41 |
| PC (30:1) | Positive | 704.5 | 184.1 | 12-41 |
| PC (30:2) | Positive | 702.5 | 184.1 | 12-41 |
| PC (32:0) | Positive | 734.6 | 184.1 | 12-41 |
| PC (32:2) | Positive | 730.5 | 184.1 | 12-41 |
| PC (32:3) | Positive | 728.5 | 184.1 | 12-41 |
| PC (34:0) | Positive | 762.6 | 184.1 | 12-41 |
| PC (34:1) | Positive | 760.6 | 184.1 | 12-41 |
| PC (34:2) | Positive | 758.6 | 184.1 | 12-41 |
| PC (34:3) | Positive | 756.6 | 184.1 | 12-41 |
| PC (34:4) | Positive | 754.5 | 184.1 | 12-41 |
| PC (36:0) | Positive | 790.6 | 184.1 | 12-41 |
| PC (36:1) | Positive | 788.6 | 184.1 | 12-41 |
| PC (36:2) | Positive | 786.6 | 184.1 | 12-41 |
| PC (36:3) | Positive | 784.6 | 184.1 | 12-41 |
| PC (36:4) | Positive | 782.6 | 184.1 | 12-41 |
| PC (36:5) | Positive | 780.6 | 184.1 | 12-41 |
| PC (38:1) | Positive | 816.6 | 184.1 | 12-41 |
| PC (38:2) | Positive | 814.6 | 184.1 | 12-41 |
| PC (38:3) | Positive | 812.6 | 184.1 | 12-41 |
| PC (38:4) | Positive | 810.6 | 184.1 | 12-41 |
| PC (38:5) | Positive | 808.6 | 184.1 | 12-41 |
| PC (38:6) | Positive | 806.6 | 184.1 | 12-41 |
| PC (38:7) | Positive | 804.6 | 184.1 | 12-41 |
| CER(16:0) | Positive | 538.6 | 264.4 | 12-41 |
| CER(18:0) | Positive | 566.7 | 264.4 | 12-41 |
| CER(18:1) | Positive | 564.8 | 264.4 | 12-41 |
| CER(20:0) | Positive | 594.6 | 264.4 | 12-41 |
| CER(22:0) | Positive | 622.7 | 264.4 | 12-41 |
| CER(24:0) | Positive | 650.8 | 264.4 | 12-41 |
| CER(24:1) | Positive | 648.8 | 264.4 | 12-41 |
| CER(26:0) | Positive | 678.9 | 264.4 | 12-41 |
| HCER(16:0) | Positive | 700.7 | 264.4 | 12-41 |
| HCER(20:0) | Positive | 756.7 | 264.4 | 12-41 |
| HCER(22:0) | Positive | 784.9 | 264.4 | 12-41 |
| HCER(24:0) | Positive | 812.9 | 264.4 | 12-41 |
| HCER(24:1) | Positive | 810.9 | 264.4 | 12-41 |
| DAG(14:0/18:1) | Positive | 584.4 | 285.2 | 12-41 |
| DAG(14:0/20:0) | Positive | 614.6 | 285.2 | 12-41 |
| DAG(16:0/18:0) | Positive | 614.4 | 313.2 | 12-41 |
| DAG(16:1/18:0) | Positive | 612.6 | 311.3 | 12-41 |
| DAG(16:0/18:1) | Positive | 612.6 | 313.2 | 12-41 |
| DAG(16:1/18:1) | Positive | 610.4 | 311.2 | 12-41 |
| DAG(18:0/18:2) | Positive | 638.4 | 341.3 | 12-41 |
| DAG(18:1/18:2) | Positive | 636.5 | 339.3 | 12-41 |
| DAG(16:0/20:3) | Positive | 636.5 | 313.3 | 12-41 |
| DAG(16:0/20:4) | Positive | 634.5 | 313.3 | 12-41 |
| DAG(18:2/18:3) | Positive | 632.4 | 337.3 | 12-41 |
| DAG(18:1/20:1) | Positive | 666.6 | 339.3 | 12-41 |
| TAG(40:0/FA14:0) | Positive | 712.6 | 467.4 | 41-65 |
| TAG(40:0/FA16:0) | Positive | 712.6 | 439.4 | 41-65 |
| TAG(42:2/FA18:2) | Positive | 736.6 | 439.4 | 41-65 |
| TAG(42:1/FA14:0) | Positive | 738.7 | 493.4 | 41-65 |
| TAG(42:1/FA16:0) | Positive | 738.7 | 465.4 | 41-65 |
| TAG(42:1/FA16:1) | Positive | 738.7 | 467.4 | 41-65 |
| TAG(42:1/FA18:1) | Positive | 738.7 | 439.4 | 41-65 |
| TAG(42:0/FA14:0) | Positive | 740.7 | 495.4 | 41-65 |
| TAG(42:0/FA16:0) | Positive | 740.7 | 467.4 | 41-65 |
| TAG(44:2/FA14:0) | Positive | 764.7 | 519.4 | 41-65 |
| TAG(44:2/FA16:0) | Positive | 764.7 | 491.4 | 41-65 |
| TAG(44:2/FA16:1) | Positive | 764.7 | 493.4 | 41-65 |
| TAG(44:2/FA18:1) | Positive | 764.7 | 465.4 | 41-65 |
| TAG(44:1/FA14:0) | Positive | 766.7 | 521.5 | 41-65 |
| TAG(44:1/FA16:0) | Positive | 766.7 | 493.4 | 41-65 |
| TAG(44:1/FA16:1) | Positive | 766.7 | 495.4 | 41-65 |
| TAG(44:1/FA18:1) | Positive | 766.7 | 467.4 | 41-65 |
| TAG(44:0/FA14:0) | Positive | 768.7 | 523.5 | 41-65 |
| TAG(44:0/FA16:0) | Positive | 768.7 | 495.4 | 41-65 |
| TAG(44:0/FA18:0) | Positive | 768.7 | 467.4 | 41-65 |
| TAG(46:1/FA16:1) | Positive | 794.7 | 523.5 | 41-65 |
| TAG(46:0/FA16:0) | Positive | 796.7 | 523.5 | 41-65 |
| TAG(48:2)\_FA 16:1 | Positive | 820.8 | 549.8 | 41-65 |
| TAG(48:2)\_FA 18:1 | Positive | 820.8 | 521.8 | 41-65 |
| TAG(48:2)\_FA 18:2 | Positive | 820.8 | 523.8 | 41-65 |
| TAG(48:2)\_FA 16:0 | Positive | 820.8 | 547.8 | 41-65 |
| TAG(48:1)\_FA 16:0 | Positive | 822.8 | 549.8 | 41-65 |
| TAG(48:1)\_FA 18:1 | Positive | 822.8 | 523.8 | 41-65 |
| TAG(48:1)\_FA 16:1 | Positive | 822.8 | 551.8 | 41-65 |
| TAG(48:0)\_FA 16:0 | Positive | 824.8 | 551.8 | 41-65 |
| TAG(48:0)\_FA 18:0 | Positive | 824.8 | 523.8 | 41-65 |
| TAG(48:0)\_FA 18:2 | Positive | 824.8 | 527.8 | 41-65 |
| TAG(50:4)\_FA 16:0 | Positive | 846.8 | 573.8 | 41-65 |
| TAG(50:4)\_FA 18:1 | Positive | 846.8 | 547.8 | 41-65 |
| TAG(50:4)\_FA 18:2 | Positive | 846.8 | 549.8 | 41-65 |
| TAG(50:4)\_FA 16:1 | Positive | 846.8 | 575.8 | 41-65 |
| TAG(50:3)\_FA 16:0 | Positive | 848.8 | 575.8 | 41-65 |
| TAG(50:3)\_FA 18:1 | Positive | 848.8 | 549.8 | 41-65 |
| TAG(50:3)\_FA 18:2 | Positive | 848.8 | 551.8 | 41-65 |
| TAG(50:3)\_FA 16:1 | Positive | 848.8 | 577.8 | 41-65 |
| TAG(50:2)\_FA 16:1 | Positive | 850.8 | 579.8 | 41-65 |
| TAG(50:2)\_FA 18:0 | Positive | 850.8 | 549.8 | 41-65 |
| TAG(50:2)\_FA 18:1 | Positive | 850.8 | 551.8 | 41-65 |
| TAG(50:2)\_FA 16:0 | Positive | 850.8 | 577.8 | 41-65 |
| TAG(50:0)\_FA 16:0 | Positive | 852.8 | 579.8 | 41-65 |
| TAG(50:1)\_FA 18:0 | Positive | 852.8 | 551.8 | 41-65 |
| TAG(50:1)\_FA 18:1 | Positive | 852.8 | 553.8 | 41-65 |
| TAG(52:5)\_FA 20:4 | Positive | 870.8 | 549.8 | 41-65 |
| TAG(52:4)\_FA 16:0 | Positive | 872.8 | 599.8 | 41-65 |
| TAG(52:4)\_FA 18:1 | Positive | 872.8 | 573.8 | 41-65 |
| TAG(52:4)\_FA 18:2 | Positive | 872.8 | 575.8 | 41-65 |
| TAG(52:4)\_FA 20:4 | Positive | 872.8 | 551.8 | 41-65 |
| TAG(52:3)\_FA 16:0 | Positive | 874.8 | 601.8 | 41-65 |
| TAG(52:3)\_FA 16:1 | Positive | 874.8 | 603.8 | 41-65 |
| TAG(52:3)\_FA 18:1 | Positive | 874.8 | 575.8 | 41-65 |
| TAG(52:3)\_FA 18:2 | Positive | 874.8 | 577.8 | 41-65 |
| TAG(52:2)\_FA 16:0 | Positive | 876.8 | 603.8 | 41-65 |
| TAG(52:2)\_FA 16:1 | Positive | 876.8 | 605.8 | 41-65 |
| TAG(52:2)\_FA 18:0 | Positive | 876.8 | 575.8 | 41-65 |
| TAG(52:2)\_FA 18:2 | Positive | 876.8 | 579.8 | 41-65 |
| TAG(52:2)\_FA 18:1 | Positive | 876.8 | 577.8 | 41-65 |
| TAG(52:1)\_FA 16:0 | Positive | 878.8 | 605.8 | 41-65 |
| TAG(52:1)\_FA 18:0 | Positive | 878.8 | 577.8 | 41-65 |
| TAG(52:1)\_FA 18:1 | Positive | 878.8 | 579.8 | 41-65 |
| TAG(52:0)\_FA 16:0 | Positive | 880.8 | 607.8 | 41-65 |
| TAG(52:0)\_FA 18:0 | Positive | 880.8 | 579.8 | 41-65 |
| TAG(52:0)\_FA 18:1 | Positive | 880.8 | 581.8 | 41-65 |
| TAG(54:7)\_FA 18:0 | Positive | 892.7 | 591.7 | 41-65 |
| TAG(54:7)\_FA 18:1 | Positive | 892.7 | 593.7 | 41-65 |
| TAG(54:4)\_FA 18:2 | Positive | 900.8 | 603.8 | 41-65 |
| TAG(54:4)\_FA 18:1 | Positive | 900.8 | 601.8 | 41-65 |
| TAG(54:3)\_FA 16:0 | Positive | 902.8 | 629.8 | 41-65 |
| TAG(54:3)\_FA 18:0 | Positive | 902.8 | 601.8 | 41-65 |
| TAG(54:3)\_FA 18:2 | Positive | 902.8 | 605.8 | 41-65 |
| TAG(54:3)\_FA 18:1 | Positive | 902.8 | 603.8 | 41-65 |
| TAG(54:2)\_FA 16:0 | Positive | 904.8 | 631.8 | 41-65 |
| TAG(54:2)\_FA 18:0 | Positive | 904.8 | 603.8 | 41-65 |
| TAG(54:2)\_FA 18:1 | Positive | 904.8 | 605.8 | 41-65 |
| TAG(54:1)\_FA 16:0 | Positive | 906.8 | 633.8 | 41-65 |
| TAG(54:1)\_FA 18:0 | Positive | 906.8 | 605.8 | 41-65 |
| TAG(54:1)\_FA 18:1 | Positive | 906.8 | 607.8 | 41-65 |
| TAG(54:0)\_FA 18:0 | Positive | 908.9 | 607.9 | 41-65 |
| TAG(56:3)\_FA 18:1 | Positive | 930.8 | 631.8 | 41-65 |
| TAG(58:3)\_FA 18:1 | Positive | 958.9 | 659.9 | 41-65 |
| TAG(60:2)\_FA 18:1 | Positive | 988.9 | 689.9 | 41-65 |
| TAG(60:2)\_FA 20:0 | Positive | 988.9 | 659.9 | 41-65 |
| TAG(60:0)\_FA 20:0 | Positive | 992.9 | 663.9 | 41-65 |