**Supporting Information**

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**Supplementary Fig. 1. Changes in IGF, HGF, EGF, and ANGPT signaling in HCVcpTg mice**

**(A)** Hepatic mRNA levels of *Igfs* and *Igfrs* were quantified by qPCR, normalized to 18S rRNA, and expressed as values relative to HCVcpTg mice fed a control diet. The number of mice in the control diet-fed and Chol-, SFA-, and TFA-rich diet-fed groups was 8, 7, 8, and 8, respectively.

**(B)** Serum IGF1 concentrations. The samples from 3 mice in each group were adopted.

**(C)** Hepatic mRNA levels of genes involved in HGF, EGF, and ANGPT signaling were quantified by qPCR, normalized to 18S rRNA, and expressed as values relative to HCVcpTg mice fed a control diet. The number of mice in the control diet-fed and Chol-, SFA-, and TFA-rich diet-fed groups was 8, 7, 8, and 8, respectively.

Data are expressed as the mean ± SD. \**P* < 0.05, \*\**P* < 0.01, and \*\*\**P* < 0.001 between control diet-fed and Chol-, SFA-, and TFA-rich diet-fed HCVcpTg mice. Con, control diet-fed HCVcpTg mice; Chol, Chol-rich diet-fed HCVcpTg mice; SFA, SFA-rich diet-fed HCVcpTg mice; TFA, TFA-rich diet-fed HCVcpTg mice.

グラフ

自動的に生成された説明

**Supplementary Table 1. Primer pairs used for qPCR analysis**

|  |  |  |
| --- | --- | --- |
| **Gene** | **Accession #** | **Primer sequence (5'-3')** |
| *18S rRNA* | NR\_003278 | F 5'-CACGGACAGGATTGACAGATTG-3' |
|  |  | R 5'-CAGACAAATCGCTCCACCAA-3' |
| *Angpt1* | NM\_009640 | F 5'-CCTGCAGAAGCAACAACTGG-3' |
|  |  | R 5'-TTTCCTCCCTTTAGCAAAACACC-3' |
| *Angpt2* | NM\_007426 | F 5'-TCGCTGGTGAAGAGTCCAAC-3' |
|  |  | R 5'-GTCAAACCACCAGCCTCCTG-3' |
| *Arnt* | NM\_009709 | F 5'-GGCGACTACAGCTAACCCAG-3' |
|  |  | R 5'-CAGCTCCTCCACCTTGAATC-3' |
| *Bach1* | NM\_007520 | F 5'-TGACAGCGAGTCCTGTTCTG-3' |
|  |  | R 5'-TTATCCGTTGGGCATTGAA-3' |
| *Bach2* | NM\_001109661 | F 5'-TATCACAAGATTGCCTCA-3' |
|  |  | R 5'-CTTCTCATCCACAGACAT-3' |
| *Cd31* | NM\_008816 | F 5'-GGAAGTGTCCTCCCTTGAGC-3' |
|  |  | R 5'-GAGCCTTCCGTTCTTAGGGTC-3' |
| *Cd34* | NM\_133654 | F 5'-GTCACCTCTGGAGTTCTGCTG-3' |
|  |  | R 5'-AGGGTCTTCACCCAGCCTTT-3' |
| *Efnb2* | NM\_010111 | F 5'-GAGGGACTCTGTGTGGAAGT-3' |
|  |  | R 5'-TCCGGGTAGAAATTTGGAGTTCG-3' |
| *Egfr* | NM\_207655 | F 5'-GCCATCTGGGCCAAAGATACC-3' |
|  |  | R 5'-GTCTTCGCATGAATAGGCCAAT-3' |
| *Fgf1* | NM\_010197 | F 5'-CCCTGACCGAGAGGTTCAAC-3' |
|  |  | R 5'-GTCCCTTGTCCCATCCACG-3' |
| *Fgf15* | NM\_008003 | F 5'-ATGGCGAGAAAGTGGAACGG-3’ |
|  |  | R 5'-CTGACACAGACTGGGATTGCT-3’ |
| *Fgf2* | NM\_008006 | F 5'-GCGACCCACACGTCAAACTA-3' |
|  |  | R 5'-TCCCTTGATAGACACAACTCCTC-3' |
| *Fgfr1* | *NM\_010206* | F 5'-TCACAGCCACTCTCTGCACT-3’ |
|  |  | R 5'-GTGGACCAGGAGAGACTCCA -3’ |
| *Fgfr2* | *NM\_201601* | F 5'-ACCACACCTACCACCTCGAT-3' |
|  |  | R 5'-GACAAACTCCACATCCCCTC-3' |
| *Fgfr3* | NM\_008010 | F 5'-GCCTGCGTGCTAGTGTTCT-3' |
|  |  | R 5'-TACCATCCTTAGCCCAGACCG-3' |
| *Fgfr4* | *NM\_008011* | F 5'-CAGAGGCCTTTGGTATGGAT-3' |
|  |  | R 5'-CAGGTCTGCCAAATCCTTGT-3' |
| *Fos* | NM\_010234 | F 5'-TCCTACTACCATTCCCCAGC-3' |
|  |  | R 5'-TGGCACTAGAGACGGACAGA-3' |
| *Hgf* | NM\_001289458 | F 5'-TGATTCTTTCAGCCCGGCAT-3' |
|  |  | R 5'-TGTCCTTCTGCATAGGGGATG-3' |
| *Hif1a* | NM\_010431 | F 5'-CCTGCACTGAATCAAGAGGTGC-3' |
|  |  | R 5'-CCATCAGAAGGACTTGCTGGCT-3' |
| *Igf1* | NM\_010512 | F 5'-AGATCTGCCTCTGTGACTTCTTG-3' |
|  |  | R 5’-TAGCCTGTGGGCTTGTTGAAG-3’ |
| *Igf1r* | NM\_010513 | F 5'-GCACCAATGCTTCAGTCCCT-3’ |
|  |  | R 5'-TTGGAGCAGTAGTTGTGCCG-3’ |
| *Igf2* | NM\_010514 | F 5'-GTTCTGTCCCGTCGCACATT-3’ |
|  |  | R 5'-CCATTGGTACCTGGAAGCCG-3’ |
| *Igf2r* | NM\_010515 | F 5'-GTCATCAGCTTTGTGTGCCG-3’ |
|  |  | R 5'-ACAGTACACTCCGTCGCTTG-3’ |
| *Jnk1* | NM\_016700 | F 5'- AGCCGTCTCCTTTAGCACAG-3’ |
|  |  | R 5'- TGTATCCGAGGCCAAAGTCG-3’ |
| *Jnk2* | NM\_0169611 | F 5'- AAGACCAGCCTTCAGCACAG-3’ |
|  |  | R 5'- TTGAGGCATCGAGACTGCTG-3’ |
| *Jun* | NM\_010591 | F 5'- CCTTCTACGACGATGCCCTC-3’ |
|  |  | R 5'- GGTTCAAGGTCATGCTCTGTTT-3’ |
| *Kit* | NM\_021099 | F 5'-GCATTTAAAGAGCAAATCCAGGC-3’ |
|  |  | R 5'-GCACCATCACAATGATCCCC-3’ |
| *Lyve1* | NM\_053247 | F 5'-ACTTGCAGCTATGGATGGGTT-3’ |
|  |  | R 5'-AGGTGTCGGATGAGTTGTGG-3’ |
| *Met* | NM\_008591 | F 5'-CCAGCCCCTCTGCTTTCTTT-3’ |
|  |  | R 5'-GAGTTGATCACATGCCAAGCG-3’ |
| *Pdgfa* | NM\_008808 | F 5'-TAACACCAGCAGCGTCAAGT-3’ |
|  |  | R 5'-CTCACCTCACATCTGTCTCCTC-3’ |
| *Pdgfb* | NM\_011057 | F 5'-GATCTCTCGGAACCTCATCG-3’ |
|  |  | R 5'-GGCTTCTTTCGCACAATCTC-3’ |
| *Pdgfc* | NM\_019971 | F 5'-CCAGTCAGCCAAATGCTCCT-3’ |
|  |  | R 5'-GGATCTTGCACTCCGTTCTGT-3’ |
| *Pdgfd* | NM\_027924 | F 5'-AACCTCAGGAGAGATGAGAGC-3’ |
|  |  | R 5'-TTGGGTAGCTGTTCGGGAAG-3’ |
| *Pdgfra* | NM\_011058 | F 5'-ACACGTTTGAGCTGTCAACC-3’ |
|  |  | R 5'-CCCGACCACACAAGAACAGG-3’ |
| *Pdgfrb* | NM\_008809 | F 5'-TTCCAGGAGTGATACCAGCTT-3’ |
|  |  | R 5'-AGGGGGCGTGATGACTAGG-3’ |
| *Pdpn* | NM\_010329 | F 5'-TCAAAGCATCTGCCTTTGGAA-3’ |
|  |  | R 5'-ACTGTCTTGGCTTTGCTCCATT-3’ |
| *Prox1* | NM\_008937 | F 5'-GAAGGGCTATCACCCAATCA-3’ |
|  |  | R 5'-TGAACCACTTGATGAGCTGC-3’ |
| *Tie1* | NM\_011587 | F 5'-CCAGTCAGGATCGGGTGAAG-3’ |
|  |  | R 5'-ATCATGGCCCGGATCACTTG-3’ |
| *Tie2* | NM\_013690 | F 5'-GCCGCGGACTGACTACGAGC-3’ |
|  |  | R 5'-GGAGGAGGGAGTCCGATAGACGC-3’ |
| *Vegfa* | NM\_009505 | F 5'-GCACATAGAGAGAATGAGCTTCC-3’ |
|  |  | R 5'-CTCCGCTCTGAACAAGGCT-3’ |
| *Vegfb* | NM\_011697 | F 5'-GCCAGACAGGGTTGCCATAC-3’ |
|  |  | R 5'-GGAGTGGGATGGATGATGTCAG-3’ |
| *Vegfc* | NM\_009506 | F 5'-GAGGTCAAGGCTTTTGAAGGC-3’ |
|  |  | R 5'-CTGTCCTGGTATTGAGGGTGG-3’ |
| *Vegfd* | NM\_010216 | F 5'-TGCAAGACGAGACTCCACTG-3’ |
|  |  | R 5'-GCAGCAGCTCTCCAGACTTT-3’ |
| *Vegfr1* | NM\_010228 | F 5'-TGGCTCTACGACCTTAGACTG-3’ |
|  |  | R 5'-CAGGTTTGACTTGTCTGAGGTT-3’ |
| *Vegfr2* | NM\_010612 | F 5'-TTTGGCAAATACAACCCTTCAGA-3’ |
|  |  | R 5'-GCAGAAGATACTGTCACCACC-3’ |
| *Vegfr3* | NM\_008029 | F 5'-CTGGCAAATGGTTACTCCATGA-3’ |
|  |  | R 5'-ACAACCCGTGTGTCTTCACTG-3’ |
| *Vhl* | NM\_009507 | F 5'-ATCCACAGCTACCGAGGTCATC-3' |
|  |  | R 5'-ATCGACATTGAGGGATGGCAC-3' |

|  |
| --- |
| *F, forward sequence; R, reverse sequence.* |
| *Angpt1, angiopoietin 1* |
| *Angpt2, angiopoietin 2* |
| *Arnt, aryl hydrocarbon receptor nuclear translocator* |
| *Bach1, BTB and CNC homology 1* |
| *Bach2, BTB and CNC homology 2* |
| *Cd31, platelet endothelial cell adhesion molecule 1* |
| *Cd34, cd34* |
| *Efnb2, ephrin B2* |
| *Egfr, epidermal growth factor receptor* |
| *Fgf1, fibroblast growth factor 1* |
| *Fgf15, fibroblast growth factor 15* |
| *Fgf2, fibroblast growth factor 2* |
| *Fgfr1, fibroblast growth factor receptor 1* |
| *Fgfr2, fibroblast growth factor receptor 2* |
| *Fgfr3, fibroblast growth factor receptor 3* |
| *Fgfr4, fibroblast growth factor receptor 4* |
| *Fos, FBJ osteosarcoma oncogene* |
| *Hgf, hepatocyte growth factor* |
| *Hif1a, hypoxia-inducible factor 1 alpha* |
| *Igf1, insulin-like growth factor 1* |
| *Igf1r, insulin-like growth factor 1 receptor* |
| *Igf2, insulin-like growth factor 2* |
| *Igf2r, insulin-like growth factor 2 receptor* |
| *Jnk1, mitogen-activated protein kinase 8* |
| *Jnk2, mitogen-activated protein kinase 9* |
| *Jun, jun proto-oncogene* |
| *Kit, c-kit* |
| *Lyve1, lymphatic vessel endothelial hyaluronan receptor 1* |
| *Met, c-met* |
| *Pdgfa, platelet-derived growth factor a* |
| *Pdgfb, platelet-derived growth factor b* |
| *Pdgfc, platelet-derived growth factor c* |
| *Pdgfd, platelet-derived growth factor d* |
| *Pdgfra, platelet-derived growth factor receptor a* |
| *Pdgfrb, platelet-derived growth factor receptor b* |
| *Pdpn, podoplanin* |
| *Prox1, prospero homeobox 1* |
| *Tie1, tyrosine kinase with immunoglobulin-like and EGF-like domains 1* |
| *Tie2, TEK receptor tyrosine kinase* |
| *Vegfa, vascular endothelial growth factor a* |
| *Vegfb, vascular endothelial growth factor b* |
| *Vegfc, vascular endothelial growth factor c* |
| *Vegfd, vascular endothelial growth factor d* |
| *Vegfr1, vascular endothelial growth factor receptor 1* |
| *Vegfr2, vascular endothelial growth factor receptor 2* |
| *Vegfr3, vascular endothelial growth factor receptor 3* |
| *Vhl, von Hippel-Lindau tumor suppressor* |

**Supplementary Table 2. Primary antibodies used for immunoblot analysis**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| Protein name | Abbreviation | Manufacturer | Catalog # | Dilution |
| Extracellular Regulated Protein Kinase | ERK | Upstate cell signaling (Lake Placid, NY) | #06-182 | 1:1000 |
| Fibroblast Growth  Factor 2 | FGF2 | Santa Cruz Biotechnology (Dallas, TX) | #sc-74412 | 1:500 |
| Fibroblast Growth  Factor Receptor 2 | FGFR2 | Santa Cruz Biotechnology (Dallas, TX) | #sc-6930 | 1:500 |
| Fibroblast Growth  Factor Receptor 3 | FGFR3 | Santa Cruz Biotechnology (Dallas, TX) | #sc-390423 | 1:500 |
| Glyceraldehyde-3-Phosphate Dehydrogenase | GAPDH | Abcam (Cambridge, MA) | #ab9485 | 1:2500 |
| Hypoxia-Inducible  Factor 1 Subunit Alpha | HIF1α | Santa Cruz Biotechnology (Dallas, TX) | #sc-10790 | 1:500 |
| c-Jun N-Terminal Kinase | JNK | Santa Cruz Biotechnology (Dallas, TX) | #sc-571 | 1:1000 |
| Lymphatic Vessel Endothelial Hyaluronan Receptor 1 | LYVE1 | Santa Cruz Biotechnology (Dallas, TX) | #sc-65647 | 1:500 |
| Platelet And Endothelial Cell Adhesion Molecule 1 | CD31 | Dianova GmbH (Hamburg, Germany) | #DIA-310 | 1:5000 |
| p38 MAPK | p38 | GeneTex, Inc.  (Irvine, USA) | #191819 | 1:1000 |
| Phospho-p38 MAPK | p-p38 | Cell Signaling Technology (Danvers, MA) | #9211 | 1:1000 |
| Phospho-Extracellular Regulated Protein Kinase | p-ERK | Cell Signaling Technology (Danvers, MA) | #4370 | 1:2000 |
| Phospho-c-Jun N-Terminal Kinase | p-JNK | Cell Signaling Technology (Danvers, MA) | #4668 | 1:1000 |
| Platelet-Derived Growth Factor Receptor Alpha | PDGFR-α | Santa Cruz Biotechnology (Dallas, TX) | #sc-398206 | 1:500 |
| Platelet-Derived Growth Factor Subunit B | PDGF-B | Santa Cruz Biotechnology (Dallas, TX) | #sc-365805 | 1:500 |
| TIE2 | TIE2 | Santa Cruz Biotechnology (Dallas, TX) | #sc-293414 | 1:500 |
| Vascular Endothelial Growth Factor C | VEGF-C | Santa Cruz Biotechnology (Dallas, TX) | #sc-374628 | 1:500 |
| Vascular Endothelial Growth Factor Receptor 2 | VEGFR2 | Santa Cruz Biotechnology (Dallas, TX) | #sc-6251 | 1:500 |

**Supplementary Table 3. Components of the diets used in the study.**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | Control diet | SFA-rich diet | TFA-rich diet | Chol-rich diet |
| Casein | 200 | 200 | 200 | 200 |
| L-Cystine | 3 | 3 | 3 | 3 |
| Corn starch | 397.486 | 332.5 | 397.486 | 380.986 |
| α-Corn starch | 132 | 132 | 0 | 132 |
| Maltodextrin | 0 | 0 | 132 | 0 |
| Sucrose | 100 | 100 | 100 | 100 |
| Cellulose | 50 | 50 | 50 | 50 |
| t-Butylhydroquinone | 0.014 | 0 | 0.014 | 0.014 |
| Mineral mix | 35 | 35 | 35 | 35 |
| Vitamin mix | 10 | 10 | 10 | 10 |
| Choline bitartrate | 2.5 | 2.5 | 2.5 | 2.5 |
| Soybean oil | 70 | 0 | 10 | 70 |
| Primex | 0 | 0 | 60 | 0 |
| Hydrogenated coconut oil | 0 | 135 | 0 | 0 |
| Cholesterol | 0 | 0 | 0 | 15 |
| Sodium cholate | 0 | 0 | 0 | 1.5 |
|  | | | | |
| Values indicate g/kg of diet. | | | | |