Dataset of the human homologues and orthologues of lipid-metabolic genes identified as DAF-16 targets their roles in lipid and energy metabolism

Lavender Yuen-Nam Fan, Paula Saavedra-García, Eric Wing-Fai Lam*

Department of Surgery and Cancer, Imperial College London, Hammersmith Hospital Campus, London W12 0NN, UK

Abstract

The data presented in this article are related to the review article entitled 'Unravelling the role of fatty acid metabolism in cancer through the FOXO3-FOXM1 axis' (Saavedra-García et al., 2017) [24]. Here, we have matched the DAF-16/FOXO3 downstream genes with their respective human orthologues and reviewed the roles of these targeted genes in FA metabolism. The list of genes listed in this article are precisely selected from literature reviews based on their functions in mammalian FA metabolism. The nematode Caenorhabditis elegans gene orthologues of the genes are obtained from WormBase, the online biological database of C. elegans. This dataset has not been uploaded to a public repository yet.

© 2017 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY license (http://creativecommons.org/licenses/by/4.0/).

Abbreviations: ACAA2, Acetyl-CoA acetyltransferase 2; ACACA, Acetyl-CoA carboxylase; ACAD8, Acyl-CoA dehydrogenase family member 8; ACADM, Acyl-CoA dehydrogenase C4 to C12 straight chain; ACSL3/4, Acyl-CoA synthetase long-chain family member 3/4; ACS2, Acyl-CoA synthetase short-chain family member; CPT2, Carnitine palmitoyltransferase II; DAG, Diacylglycerol; DGAT, Diacylglycerol O-acyltransferase; ECHS1, Short-chain enoyl-CoA hydratase 1; ELOVL1, Elongation of very long chain fatty acids protein 1; FA, Fatty acid; FADS2, Fatty acid desaturase 2; FASN, Fatty acid synthase; FABP4, Fatty acid transport protein 4; FOX, Forkhead box; HADH, Hydroxyacyl-coenzyme A dehydrogenase; HADHA, Hydroxyacyl-CoA dehydrogenase/3-Ketoacyl-CoA thiolase/Enoyl-CoA hydratase, alpha subunit; LCFA, Long chain fatty acid; MLYCD, Malonyl-CoA decarboxylase; MOGAT1/2, Monoacylglycerol O-acyltransferase 1/2; PNPLA, patatin like phospholipase domain containing; PUFA, polyunsaturated fatty acid; SCD1/5, Stearoyl-CoA desaturase 1/5; TAG, triacylglycerol; TCA, Tri-carboxylic acid; VLCFA, Very long chain fatty acid.

* Corresponding author.

E-mail address: eric.lam@imperial.ac.uk (E.-F. Lam).
The dataset shows the extensive overlap in the signaling pathway and molecules involved in the FOXO3-FOXM1 axis and FA metabolism. The assessment of this interaction can be of value for research groups from related fields.

The dataset allows integration of researches in oncology and metabolic diseases.

The dataset opens up new approaches to study the roles of FOXO3-FOXM1 axis and FA metabolism in breast cancer initiation, progression and metastasis and drug resistance.

These data also be useful for researches in all cancer types where lipid and energy metabolism is implicated.

1. Data

Based on literature reviews, we observed that the DAF-16 is the *C. elegans* orthologues of mammalian forkhead box (FOX) proteins, FOXO3 and FOXM1, and also the primary factor essential for enhancing the expression of gene networks involved in regulation of fatty acid (FA) metabolism [1, 5, 9, 24, 25]. The dataset of this article provides information of the genes that are overlapped in cellular pathways involved in both FOXO3-FOXM1 axis and FA metabolism [4, 13, 18, 35]. From Amrit et al., we selected a list of FA metabolism regulatory genes that are downstream of DAF-16/FOXO3 [1]. To better understand the roles of FOXO3-FOXM1 axis in FA metabolism, we then matched the genes with their respective human orthologues using WormBase (www.wormbase.org), and their roles in lipid and energy metabolism are summarized in Table 1.

| C. elegans genes regulated by DAF-16/FOXO3 | Human orthologues (from WormBase) [27] | Role in lipid and energy metabolism |
|------------------------------------------|----------------------------------------|-----------------------------------|
| pod-2                                    | Acetyl-CoA carboxylase alpha (ACACA)   | The major regulatory enzyme involved in rate-limiting step of de novo FA biosynthesis [11]. ACACA promotes FA biosynthesis by catalyzing the conversion of acetyl-CoA to Malonyl-CoA, a building block of FA [11]. |
| mlcd-1                                   | Malonyl-CoA decarboxylase (MLYCD)      | An enzyme that produces acetyl-CoA from malonyl-CoA [14], thus increase the rate of β-oxidation. |
| fasn-1                                   | Fatty acid synthase (FASN)             | The major regulatory enzyme that mediates the de novo synthesis of saturated FAs from acetyl-CoA and malonyl-CoA [2]. |
| C. elegans genes regulated by DAF-16/FOXO3 | Human orthologues (from WormBase) [27] | Role in lipid and energy metabolism |
|-----------------------------------------|------------------------------------------|----------------------------------|
| mboa-2 | Diacylglycerol O-acyltransferase (DGAT) 1 | One of 2 enzymes that catalyze the final step in triacylglycerol (TAG) synthesis in which diacylglycerol (DAG) is covalently bound to long chain fatty acyl-CoAs [20]. |
| dgat-2 | DGAT2 | The second enzymes that catalyze the final reaction in the synthesis of TAG [28]. |
| acs-22 | Fatty acid transport protein 4 (FATP4) | The membrane transporter essential for translocation of very long chain fatty acid (VLCFA) across the plasma membrane into cells [6]. |
| Y53G8B.2, K07B1.4 | Monoacylglycerol O-acyltransferase 1/2 (MOGAT1/2), DGAT2 | Enzymes predicted to have transferase activity, transferring acyl groups other than amino-acyl groups [28] and catalyze the synthesis of DAGs, precursor of TAGs and phospholipids [34]. Integral membrane proteins of the endoplasmic reticulum that catalyzes the formation of mono-unsaturated FAs from saturated FAs, a key regulator of energy metabolism [30]. |
| fat-5, fat-6, fat-7 | Stearoyl-CoA desaturase 1/5 (SCD1/5) | Proteins involved in lipid (cholesteryl ester) storage; lip-1 and lip-2 are predicted to have hydrolase activity, acting on ester bonds of cholesteryl esters and TAGs [23]. |
| lipl-1, lipl-2, lipl-5 | Lipase A (orthologue of lip-1), Lipase F, gastric type (orthologue of lipl-1 and lipl-2), and other members of the Lipases family | Proteins that have diverse lipolytic and acyltransferase activities and are key elements in lipid metabolism [12]. |
| atgl-1 | Patatin like phospholipase domain containing (PNPLA) 1, PNPLA2 and PNPLA3 | Proteins involved in lipid (cholesteryl ester) storage; lip-1 and lip-2 are predicted to have hydrolase activity, acting on ester bonds of cholesteryl esters and TAGs [23]. |
| acoa-1 | Acyl-CoA oxidase 1 (ACOX1) | The enzyme catalyzes the first, rate-limiting step in peroxisomal β-oxidation of medium to very long straight-chain FA [17]. |
| ech-7 | Short-chain enoyl-CoA hydratase (ECHS1) | Enzyme functions in the second step of the mitochondrial β-oxidation pathway. It catalyzes the hydration of 2-trans-enoyl-coenzyme A intermediates to L-3-hydroxyacyl-CoAs [8]. |
| ech-1.2 | Hydroxyacyl-CoA Dehydrogenase/3-Ketoacyl-CoA Thiolase/Enoyl-CoA Hydratase, Alpha Subunit (HADHA) | The tri-functional protein that catalyzes the last three steps of mitochondrial β-oxidation of LCFAs [22]. |
| acdh-1 | Hydroxyacyl-coenzyme A dehydrogenase (HADH) | A mitochondrial enzyme catalyzes the alpha, beta-dehydrogenation of acyl-CoA derivatives in the metabolism of FAs or branch chained amino acid [20,29]. |
| acoa-2 | Acetyl-CoA acetyltransferase 2(ACAA2) | An enzyme involved in the last step of mitochondrial β-oxidation [19]. |
| hacd-1 | Hydroxyacyl-coenzyme A dehydrogenase (HADH) | An enzyme involved in the last step of mitochondrial β-oxidation [19]. |
| cpt-2 | Carnitine palmitoyltransferase II (CPT2) | Transporter protein at mitochondrial inner membrane that catalyzes an acyl-group transfer between added CoA and carnitine [32], thus facilitates β-oxidation pathway in the mitochondria. |
| acdl-9 | Acyl-CoA dehydrogenase family, member 8 (ACAD8) | A mitochondrial enzyme catalyzes the alpha, beta-dehydrogenation of acyl-CoA derivatives in the metabolism of FAs or branch chained amino acid [20,29]. |
| ech-1.2 | Hydroxyacyl-CoA Dehydrogenase/3-Ketoacyl-CoA Thiolase/Enoyl-CoA Hydratase, Alpha Subunit (HADHA) | The tri-functional protein that catalyzes the last three steps of mitochondrial β-oxidation of LCFAs [22]. |
| acdh-1 | Hydroxyacyl-coenzyme A dehydrogenase (HADH) | A mitochondrial enzyme catalyzes the alpha, beta-dehydrogenation of acyl-CoA derivatives in the metabolism of FAs or branch chained amino acid [20,29]. |
Table 1 (continued)

| C. elegans genes regulated by DAF-16/FOXO3 | Human orthologues (from WormBase) [27] | Role in lipid and energy metabolism |
|-----------------------------------------|----------------------------------------|-----------------------------------|
| fat-2                                   | Fatty acid desaturase 2 (FADS2)        | A delta-12 fatty acyl desaturase that catalyzes the formation of double bond between defined carbons of fatty acyl chain [10]. |
| acs-2                                   | Members of Acyl-CoA synthetase family, such as acyl-CoA Synthetase Short-Chain Family member (ACSS) 1, ACSS2 and ACSS3 | Enzymes predicted to catalyze the conversion of acetate to acetyl-CoA in order for it to fuel the tricarboxylic acid (TCA) cycle to produce ATP [27]. Microsomal enzymes involved in VLCFA elongation during increased β-oxidation [7,21]. |
| elo-1, elo-2                            | Polysaturated fatty acid (PUFA) elongases, such as Elongation of very long chain fatty acids protein 1 (ELOVL1) | Very-long-chain specific acyl-CoA dehydrogenase that catalyze the initial step of the mitochondrial β-oxidation, specific to C4 to C12 straight chain [16]. |
| acdh-11                                 | Acyl-CoA dehydrogenase family members, such as Acetyl-CoA Dehydrogenase C4 to C12 Straight Chain (ACADM) | Pseudogenes of lipl-1, -2 and -5, proteins predicted to have hydrolase and lipid storage activity [27]. |

Acknowledgements

Lavender Yuen-Nam Fan is a PhD student and research assistant supported by Imperial College IC Trust. Paula Saavedra-Garcia is a post-doctoral research associate supported by the Medical Research Council (MRC) of UK (MR/N012097/1). Eric W.-F. Lam’s work is supported by MRC (MR/N012097/1), CRUK (A12011) and Breast Cancer Now (2012MayPR070; 2012NovPhD016).

Transparency document. Supplementary material

Transparency data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.dib.2017.02.055.

References

[1] F.R. Amrit, E.M. Steenkiste, R. Ratnappan, S.W. Chen, T.B. McClendon, D. Kostka, J. Yanowitz, C.P. Olsen, A. Ghazi, DAF-16 and TCE-1 facilitate adaptation to germline loss by restoring lipid homeostasis and repressing reproductive physiology in C. elegans, PLoS Genet. 12 (2016) e1005788.
[2] S.S. Chirala, H. Chang, M. Matzuk, L. Abu-Elheiga, J. Mao, K. Mahon, M. Finegold, S.J. Wakil, Fatty acid synthesis is essential in embryonic development: fatty acid synthase null mutants and most of the heterozygotes die in utero, Proc. Natl. Acad. Sci. USA 100 (2003) 6358–6363.
[3] D.J. Durgan, J.K. Smith, M.A. Hotze, O. Egbejimi, K.D. Cuthbert, V.G. Zaha, J.R. Dyck, E.D. Abel, M.E. Young, Distinct transcriptional regulation of long-chain acyl-CoA synthetase isoforms and cytosolic thioesterase 1 in the rodent heart by fatty acids and insulin, Am. J. Physiol. Heart Circ. Physiol. 290 (2006) H2480–H2497.
[4] D.N. Gross, A.P. van den Heuvel, M.J. Birnbaum, The role of FoxO in the regulation of metabolism, Oncogene 27 (2008) 2320–2336.
[5] S. Hannenhalli, K.H. Kaestner, The evolution of Fox genes and their role in development and disease, Nat. Rev. Genet. 10 (2009) 233–240.
[6] T. Herrmann, F. Buchkremer, I. Gosch, A.M. Hall, D.A. Bernlohr, W. Stremmel, Mouse fatty acid transport protein 4 (FATP4): characterization of the gene and functional assessment as a very long chain acyl-CoA synthase, Gene 270 (2001) 31–40.
[7] A. Jakobsson, J.A. Jorgensen, A. Jacobsen, Differential regulation of fatty acid elongation enzymes in brown adipocytes implies a unique role for Elovl3 during increased fatty acid oxidation, Am. J. Physiol. Endocrinol. Metab. 289 (2005) E517–E526.
