

## 2A. Hepatocyte nuclear factor-4 receptors in GtoPdb v.2023.1

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### Abstract

The nomenclature of hepatocyte nuclear factor-4 receptors is agreed by the **NC-IUPHAR Subcommittee on Nuclear Hormone Receptors [9, 3]**. While linoleic acid has been identified as the endogenous ligand for HNF4 $\alpha$  its function remains ambiguous [75]. HNF4 $\gamma$  has yet to be paired with an endogenous ligand.

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### Database links

#### 2A. Hepatocyte nuclear factor-4 receptors

<https://www.guidetopharmacology.org/GRAC/FamilyDisplayForward?familyId=91>

#### Introduction to 2A. Hepatocyte nuclear factor-4 receptors

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#### Receptors

##### Hepatocyte nuclear factor-4- $\alpha$

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=608>

##### Hepatocyte nuclear factor-4- $\gamma$

<https://www.guidetopharmacology.org/GRAC/ObjectDisplayForward?objectId=609>

### References

1. Aguilar-Salinas CA, Reyes-Rodríguez E, Ordóñez-Sánchez ML, Torres MA, Ramírez-Jiménez S, Domínguez-López A, Martínez-Francois JR, Velasco-Pérez ML, Alpizar M, García-García E, Gómez-Pérez F, Rull J and Tusié-Luna MT. (2001) Early-onset type 2 diabetes: metabolic and genetic characterization

- in the mexican population. *J Clin Endocrinol Metab* **86**: 220-6 [PMID:11232004]
2. Akiyama TE and Gonzalez FJ. (2003) Regulation of P450 genes by liver-enriched transcription factors and nuclear receptors. *Biochim Biophys Acta* **1619**: 223-34 [PMID:12573481]
  3. Alexander SPH, Cidlowski JA, Kelly E, Mathie A, Peters JA, Veale EL, Armstrong JF, Faccenda E, Harding SD and Pawson AJ *et al.*. (2019) THE CONCISE GUIDE TO PHARMACOLOGY 2019/20: Nuclear hormone receptors. *Br J Pharmacol* **176 Suppl 1**: S229-S246 [PMID:31710718]
  4. Arbini AA, Pollak ES, Bayleran JK, High KA and Bauer KA. (1997) Severe factor VII deficiency due to a mutation disrupting a hepatocyte nuclear factor 4 binding site in the factor VII promoter. *Blood* **89**: 176-82 [PMID:8978290]
  5. Archer A, Sauvaget D, Chauffeton V, Bouchet PE, Chambaz J, Pinçon-Raymond M, Cardot P, Ribeiro A and Lacasa M. (2005) Intestinal apolipoprotein A-IV gene transcription is controlled by two hormone-responsive elements: a role for hepatic nuclear factor-4 isoforms. *Mol Endocrinol* **19**: 2320-34 [PMID:15928313]
  6. Argyrokastritis A, Kamakari S, Kapsetaki M, Kritis A, Talianidis I and Moschonas NK. (1997) Human hepatocyte nuclear factor-4 (hHNF-4) gene maps to 20q12-q13.1 between PLCG1 and D20S17. *Hum Genet* **99**: 233-6 [PMID:9048927]
  7. Avraham KB, Prezioso VR, Chen WS, Lai E, Sladek FM, Zhong W, Darnell JE, Jenkins NA and Copeland NG. (1992) Murine chromosomal location of four hepatocyte-enriched transcription factors: HNF-3 alpha, HNF-3 beta, HNF-3 gamma, and HNF-4. *Genomics* **13**: 264-8 [PMID:1612587]
  8. Barrio R, Bellanné-Chantelot C, Moreno JC, Morel V, Calle H, Alonso M and Mustieles C. (2002) Nine novel mutations in maturity-onset diabetes of the young (MODY) candidate genes in 22 Spanish families. *J Clin Endocrinol Metab* **87**: 2532-9 [PMID:12050210]
  9. Benoit G, Cooney A, Giguere V, Ingraham H, Lazar M, Muscat G, Perlmann T, Renaud JP, Schwabe J, Sladek F, Tsai MJ and Laudet V. (2006) International Union of Pharmacology. LXVI. Orphan nuclear receptors. *Pharmacol Rev* **58**: 798-836 [PMID:17132856]
  10. Bogan AA, Dallas-Yang Q, Ruse MD, Maeda Y, Jiang G, Nepomuceno L, Scanlan TS, Cohen FE and Sladek FM. (2000) Analysis of protein dimerization and ligand binding of orphan receptor HNF4alpha. *J Mol Biol* **302**: 831-51 [PMID:10993727]
  11. Buneman P, Christie G, Davies JA, Dimitrellou R, Harding SD, Pawson AJ, Sharman JL and Wu Y. (2020) Why data citation isn't working, and what to do about it *Database* **2020** [PMID:32367113]
  12. Chartier FL, Bossu JP, Laudet V, Fruchart JC and Laine B. (1994) Cloning and sequencing of cDNAs encoding the human hepatocyte nuclear factor 4 indicate the presence of two isoforms in human liver. *Gene* **147**: 269-72 [PMID:7926813]
  13. Chen WS, Manova K, Weinstein DC, Duncan SA, Plump AS, Prezioso VR, Bachvarova RF and Darnell JE. (1994) Disruption of the HNF-4 gene, expressed in visceral endoderm, leads to cell death in embryonic ectoderm and impaired gastrulation of mouse embryos. *Genes Dev* **8**: 2466-77 [PMID:7958910]
  14. Chou WC, Prokova V, Shiraishi K, Valcourt U, Moustakas A, Hadzopoulou-Cladaras M, Zannis VI and Kardassis D. (2003) Mechanism of a transcriptional cross talk between transforming growth factor-beta-regulated Smad3 and Smad4 proteins and orphan nuclear receptor hepatocyte nuclear factor-4. *Mol Biol Cell* **14**: 1279-94 [PMID:12631740]
  15. Drewes T, Senkel S, Holewa B and Ryffel GU. (1996) Human hepatocyte nuclear factor 4 isoforms are encoded by distinct and differentially expressed genes. *Mol Cell Biol* **16**: 925-31 [PMID:8622695]
  16. Duncan SA, Manova K, Chen WS, Hoodless P, Weinstein DC, Bachvarova RF and Darnell JE. (1994) Expression of transcription factor HNF-4 in the extraembryonic endoderm, gut, and nephrogenic tissue of the developing mouse embryo: HNF-4 is a marker for primary endoderm in the implanting blastocyst. *Proc Natl Acad Sci USA* **91**: 7598-602 [PMID:8052626]
  17. Duncan SA, Nagy A and Chan W. (1997) Murine gastrulation requires HNF-4 regulated gene expression in the visceral endoderm: tetraploid rescue of Hnf-4(-/-) embryos. *Development* **124**: 279-87 [PMID:9053305]
  18. Eeckhoutte J, Moerman E, Bouckenooghe T, Lukoviak B, Pattou F, Formstecher P, Kerr-Conte J, Vandewalle B and Laine B. (2003) Hepatocyte nuclear factor 4 alpha isoforms originated from the P1 promoter are expressed in human pancreatic beta-cells and exhibit stronger transcriptional potentials than P2 promoter-driven isoforms. *Endocrinology* **144**: 1686-94 [PMID:12697672]
  19. Furuta H, Iwasaki N, Oda N, Hinokio Y, Horikawa Y, Yamagata K, Yano N, Sugahiro J, Ogata M and Ohgawara H *et al.*. (1997) Organization and partial sequence of the hepatocyte nuclear factor-4

- alpha/MODY1 gene and identification of a missense mutation, R127W, in a Japanese family with MODY. *Diabetes* **46**: 1652-7 [PMID:9313765]
20. Galson DL, Tsuchiya T, Tendler DS, Huang LE, Ren Y, Ogura T and Bunn HF. (1995) The orphan receptor hepatic nuclear factor 4 functions as a transcriptional activator for tissue-specific and hypoxia-specific erythropoietin gene expression and is antagonized by EAR3/COUP-TF1. *Mol Cell Biol* **15**: 2135-44 [PMID:7891708]
  21. Gagnoli C, Lindner T, Cockburn BN, Kaisaki PJ, Gagnoli F, Marozzi G and Bell GI. (1997) Maturity-onset diabetes of the young due to a mutation in the hepatocyte nuclear factor-4 alpha binding site in the promoter of the hepatocyte nuclear factor-1 alpha gene. *Diabetes* **46**: 1648-51 [PMID:9313764]
  22. Gupta RK and Kaestner KH. (2004) HNF-4alpha: from MODY to late-onset type 2 diabetes. *Trends Mol Med* **10**: 521-4 [PMID:15519277]
  23. Hall RK, Sladek FM and Granner DK. (1995) The orphan receptors COUP-TF and HNF-4 serve as accessory factors required for induction of phosphoenolpyruvate carboxykinase gene transcription by glucocorticoids. *Proc Natl Acad Sci USA* **92**: 412-6 [PMID:7831301]
  24. Hani EH, Suaud L, Boutin P, Chèvre JC, Durand E, Philippi A, Demenais F, Vionnet N, Furuta H, Velho G, Bell GI, Laine B and Froguel P. (1998) A missense mutation in hepatocyte nuclear factor-4 alpha, resulting in a reduced transactivation activity, in human late-onset non-insulin-dependent diabetes mellitus. *J Clin Invest* **101**: 521-6 [PMID:9449683]
  25. Hata S, Inoue T, Kosuga K, Nakashima T, Tsukamoto T and Osumi T. (1995) Identification of two splice isoforms of mRNA for mouse hepatocyte nuclear factor 4 (HNF-4). *Biochim Biophys Acta* **1260**: 55-61 [PMID:7999795]
  26. Hata S, Tsukamoto T and Osumi T. (1992) A novel isoform of rat hepatocyte nuclear factor 4 (HNF-4). *Biochim Biophys Acta* **1131**: 211-3 [PMID:1610903]
  27. Hayhurst GP, Lee YH, Lambert G, Ward JM and Gonzalez FJ. (2001) Hepatocyte nuclear factor 4alpha (nuclear receptor 2A1) is essential for maintenance of hepatic gene expression and lipid homeostasis. *Mol Cell Biol* **21**: 1393-403 [PMID:11158324]
  28. Hu C and Perlmutter DH. (1999) Regulation of alpha1-antitrypsin gene expression in human intestinal epithelial cell line caco-2 by HNF-1alpha and HNF-4. *Am J Physiol* **276**: G1181-94 [PMID:10330009]
  29. Jiang G, Nepomuceno L, Hopkins K and Sladek FM. (1995) Exclusive homodimerization of the orphan receptor hepatocyte nuclear factor 4 defines a new subclass of nuclear receptors. *Mol Cell Biol* **15**: 5131-43 [PMID:7651430]
  30. Jiang G and Sladek FM. (1997) The DNA binding domain of hepatocyte nuclear factor 4 mediates cooperative, specific binding to DNA and heterodimerization with the retinoid X receptor alpha. *J Biol Chem* **272**: 1218-25 [PMID:8995424]
  31. Kardassis D, Pardali K and Zannis VI. (2000) SMAD proteins transactivate the human ApoCIII promoter by interacting physically and functionally with hepatocyte nuclear factor 4. *J Biol Chem* **275**: 41405-14 [PMID:10995777]
  32. Kardassis D, Tzamelis I, Hadzopoulou-Cladaras M, Talianidis I and Zannis V. (1997) Distal apolipoprotein C-III regulatory elements F to J act as a general modular enhancer for proximal promoters that contain hormone response elements. Synergism between hepatic nuclear factor-4 molecules bound to the proximal promoter and distal enhancer sites. *Arterioscler Thromb Vasc Biol* **17**: 222-32 [PMID:9012660]
  33. Kiselyuk A, Lee SH, Farber-Katz S, Zhang M, Athavankar S, Cohen T, Pinkerton AB, Ye M, Bushway P and Richardson AD *et al.* (2012) HNF4 $\alpha$  antagonists discovered by a high-throughput screen for modulators of the human insulin promoter. *Chem Biol* **19**: 806-18 [PMID:22840769]
  34. Ktistaki E and Talianidis I. (1997) Modulation of hepatic gene expression by hepatocyte nuclear factor 1. *Science* **277**: 109-12 [PMID:9204893]
  35. Ktistaki E and Talianidis I. (1997) Chicken ovalbumin upstream promoter transcription factors act as auxiliary cofactors for hepatocyte nuclear factor 4 and enhance hepatic gene expression. *Mol Cell Biol* **17**: 2790-7 [PMID:9111350]
  36. Kuo CJ, Conley PB, Chen L, Sladek FM, Darnell JE and Crabtree GR. (1992) A transcriptional hierarchy involved in mammalian cell-type specification. *Nature* **355**: 457-61 [PMID:1734282]
  37. Lausen J, Thomas H, Lemm I, Bulman M, Borgschulze M, Lingott A, Hattersley AT and Ryffel GU. (2000) Naturally occurring mutations in the human HNF4alpha gene impair the function of the transcription factor to a varying degree. *Nucleic Acids Res* **28**: 430-7 [PMID:10606640]
  38. Lee YK, Dell H, Dowhan DH, Hadzopoulou-Cladaras M and Moore DD. (2000) The orphan nuclear

- receptor SHP inhibits hepatocyte nuclear factor 4 and retinoid X receptor transactivation: two mechanisms for repression. *Mol Cell Biol* **20**: 187-95 [PMID:10594021]
39. Lehto M, Bitzén PO, Isomaa B, Wipemo C, Wessman Y, Forsblom C, Tuomi T, Taskinen MR and Groop L. (1999) Mutation in the HNF-4alpha gene affects insulin secretion and triglyceride metabolism. *Diabetes* **48**: 423-5 [PMID:10334325]
  40. Lin J, Puigserver P, Donovan J, Tarr P and Spiegelman BM. (2002) Peroxisome proliferator-activated receptor gamma coactivator 1beta (PGC-1beta), a novel PGC-1-related transcription coactivator associated with host cell factor. *J Biol Chem* **277**: 1645-8 [PMID:11733490]
  41. Maeda Y, Rachez C, Hawel L, Byus CV, Freedman LP and Sladek FM. (2002) Polyamines modulate the interaction between nuclear receptors and vitamin D receptor-interacting protein 205. *Mol Endocrinol* **16**: 1502-10 [PMID:12089346]
  42. Malik S, Wallberg AE, Kang YK and Roeder RG. (2002) TRAP/SMCC/mediator-dependent transcriptional activation from DNA and chromatin templates by orphan nuclear receptor hepatocyte nuclear factor 4. *Mol Cell Biol* **22**: 5626-37 [PMID:12101254]
  43. Metzger S, Halaas JL, Breslow JL and Sladek FM. (1993) Orphan receptor HNF-4 and bZip protein C/EBP alpha bind to overlapping regions of the apolipoprotein B gene promoter and synergistically activate transcription. *J Biol Chem* **268**: 16831-8 [PMID:8344962]
  44. Mietus-Snyder M, Sladek FM, Ginsburg GS, Kuo CF, Ladias JA, Darnell JE and Karathanasis SK. (1992) Antagonism between apolipoprotein AI regulatory protein 1, Ear3/COUP-TF, and hepatocyte nuclear factor 4 modulates apolipoprotein CIII gene expression in liver and intestinal cells. *Mol Cell Biol* **12**: 1708-18 [PMID:1312668]
  45. Monney CT, Kaltenrieder V, Cousin P, Bonny C and Schorderet DF. (2002) Large Family With Maturity-Onset Diabetes of the Young and a Novel V121I Mutation in HNF4A. *Hum Mutat* **20**: 230-1 [PMID:12203996]
  46. Muller YL, Infante AM, Hanson RL, Love-Gregory L, Knowler W, Bogardus C and Baier LJ. (2005) Variants in hepatocyte nuclear factor 4alpha are modestly associated with type 2 diabetes in Pima Indians. *Diabetes* **54**: 3035-9 [PMID:16186411]
  47. Møller AM, Dalgaard LT, Ambye L, Hansen L, Schmitz O, Hansen T and Pedersen O. (1999) A novel Phe75fsdelT mutation in the hepatocyte nuclear factor-4alpha gene in a Danish pedigree with maturity-onset diabetes of the young. *J Clin Endocrinol Metab* **84**: 367-9 [PMID:9920109]
  48. Odom DT, Zizlsperger N, Gordon DB, Bell GW, Rinaldi NJ, Murray HL, Volkert TL, Schreiber J, Rolfe PA, Gifford DK, Fraenkel E, Bell GI and Young RA. (2004) Control of pancreas and liver gene expression by HNF transcription factors. *Science* **303**: 1378-81 [PMID:14988562]
  49. Oxombre B, Kouach M, Moerman E, Formstecher P and Laine B. (2004) The G115S mutation associated with maturity-onset diabetes of the young impairs hepatocyte nuclear factor 4alpha activities and introduces a PKA phosphorylation site in its DNA-binding domain. *Biochem J* **383**: 573-80 [PMID:15233628]
  50. Oxombre B, Moerman E, Eeckhoutte J, Formstecher P and Laine B. (2002) Mutations in hepatocyte nuclear factor 4alpha (HNF4alpha) gene associated with diabetes result in greater loss of HNF4alpha function in pancreatic beta-cells than in nonpancreatic beta-cells and in reduced activation of the apolipoprotein CIII promoter in hepatic cells. *J Mol Med* **80**: 423-30 [PMID:12110948]
  51. Ozeki T, Takahashi Y, Kume T, Nakayama K, Yokoi T, Nunoya K, Hara A and Kamataki T. (2001) Co-operative regulation of the transcription of human dihydrodiol dehydrogenase (DD)4/aldo-keto reductase (AKR)1C4 gene by hepatocyte nuclear factor (HNF)-4alpha/gamma and HNF-1alpha. *Biochem J* **355**: 537-44 [PMID:11284743]
  52. Parviz F, Li J, Kaestner KH and Duncan SA. (2002) Generation of a conditionally null allele of hnf4alpha. *Genesis* **32**: 130-3 [PMID:11857799]
  53. Parviz F, Matullo C, Garrison WD, Savatski L, Adamson JW, Ning G, Kaestner KH, Rossi JM, Zaret KS and Duncan SA. (2003) Hepatocyte nuclear factor 4alpha controls the development of a hepatic epithelium and liver morphogenesis. *Nat Genet* **34**: 292-6 [PMID:12808453]
  54. Price JA, Fossey SC, Sale MM, Brewer CS, Freedman BI, Wuerth JP and Bowden DW. (2000) Analysis of the HNF4 alpha gene in Caucasian type II diabetic nephropathic patients. *Diabetologia* **43**: 364-72 [PMID:10768098]
  55. Pruhova S, Ek J, Lebl J, Sumnik Z, Saudek F, Andel M, Pedersen O and Hansen T. (2003) Genetic epidemiology of MODY in the Czech republic: new mutations in the MODY genes HNF-4alpha, GCK and



- HNF-1alpha. *Diabetologia* **46**: 291-5 [PMID:12627330]
56. Rha GB, Wu G, Shoelson SE and Chi YI. (2009) Multiple binding modes between HNF4alpha and the LXXLL motifs of PGC-1alpha lead to full activation. *J Biol Chem* **284**: 35165-76 [PMID:19846556]
  57. Rowley CW, Staloch LJ, Divine JK, McCaul SP and Simon TC. (2006) Mechanisms of mutual functional interactions between HNF-4alpha and HNF-1alpha revealed by mutations that cause maturity onset diabetes of the young. *Am J Physiol Gastrointest Liver Physiol* **290**: G466-75 [PMID:16223942]
  58. Ruse MD, Privalsky ML and Sladek FM. (2002) Competitive cofactor recruitment by orphan receptor hepatocyte nuclear factor 4alpha1: modulation by the F domain. *Mol Cell Biol* **22**: 1626-38 [PMID:11865043]
  59. Ryffel GU. (2001) Mutations in the human genes encoding the transcription factors of the hepatocyte nuclear factor (HNF)1 and HNF4 families: functional and pathological consequences. *J Mol Endocrinol* **27**: 11-29 [PMID:11463573]
  60. Sauvaget D, Chauffeton V, Citadelle D, Chatelet FP, Cywiner-Golenzer C, Chambaz J, Pinçon-Raymond M, Cardot P, Le Beyec J and Ribeiro A. (2002) Restriction of apolipoprotein A-IV gene expression to the intestine villus depends on a hormone-responsive element and parallels differential expression of the hepatic nuclear factor 4alpha and gamma isoforms. *J Biol Chem* **277**: 34540-8 [PMID:12105231]
  61. Shimamoto Y, Ishida J, Yamagata K, Saito T, Kato H, Matsuoka T, Hirota K, Daitoku H, Nangaku M, Yamagata K, Fujii H, Takeda J and Fukamizu A. (2004) Inhibitory effect of the small heterodimer partner on hepatocyte nuclear factor-4 mediates bile acid-induced repression of the human angiotensinogen gene. *J Biol Chem* **279**: 7770-6 [PMID:14672953]
  62. Sladek FM, Ruse MD, Nepomuceno L, Huang SM and Stallcup MR. (1999) Modulation of transcriptional activation and coactivator interaction by a splicing variation in the F domain of nuclear receptor hepatocyte nuclear factor 4alpha1. *Mol Cell Biol* **19**: 6509-22 [PMID:10490591]
  63. Sladek FM and Seidel SD. (2001) Hepatocyte Nuclear Factor 4a. In *Nuclear Receptors and Genetic Diseases* Edited by Burris TP, McCabe ERB: Academic Press: 309-361
  64. Sladek FM, Zhong WM, Lai E and Darnell JE. (1990) Liver-enriched transcription factor HNF-4 is a novel member of the steroid hormone receptor superfamily. *Genes Dev* **4**: 2353-65 [PMID:2279702]
  65. Sugiyama T, Wang JC, Scott DK and Granner DK. (2000) Transcription activation by the orphan nuclear receptor, chicken ovalbumin upstream promoter-transcription factor I (COUP-TFI). Definition of the domain involved in the glucocorticoid response of the phosphoenolpyruvate carboxykinase gene. *J Biol Chem* **275**: 3446-54 [PMID:10652338]
  66. Tanaka T, Jiang S, Hotta H, Takano K, Iwanari H, Sumi K, Daigo K, Ohashi R, Sugai M, Ikegame C, Umezu H, Hirayama Y, Midorikawa Y, Hippo Y, Watanabe A, Uchiyama Y, Hasegawa G, Reid P, Aburatani H, Hamakubo T, Sakai J, Naito M and Kodama T. (2006) Dysregulated expression of P1 and P2 promoter-driven hepatocyte nuclear factor-4alpha in the pathogenesis of human cancer. *J Pathol* **208**: 662-72 [PMID:16400631]
  67. Taraviras S, Mantamadiotis T, Dong-Si T, Mincheva A, Lichter P, Drewes T, Ryffel GU, Monaghan AP and Schütz G. (2000) Primary structure, chromosomal mapping, expression and transcriptional activity of murine hepatocyte nuclear factor 4gamma. *Biochim Biophys Acta* **1490**: 21-32 [PMID:10786614]
  68. Thomas H, Jaschowitz K, Bulman M, Frayling TM, Mitchell SM, Roosen S, Lingott-Frieg A, Tack CJ, Ellard S, Ryffel GU and Hattersley AT. (2001) A distant upstream promoter of the HNF-4alpha gene connects the transcription factors involved in maturity-onset diabetes of the young. *Hum Mol Genet* **10**: 2089-97 [PMID:11590126]
  69. Tirona RG, Lee W, Leake BF, Lan LB, Cline CB, Lamba V, Parviz F, Duncan SA, Inoue Y, Gonzalez FJ, Schuetz EG and Kim RB. (2003) The orphan nuclear receptor HNF4alpha determines PXR- and CAR-mediated xenobiotic induction of CYP3A4. *Nat Med* **9**: 220-4 [PMID:12514743]
  70. Wang JC, Stafford JM and Granner DK. (1998) SRC-1 and GRIP1 coactivate transcription with hepatocyte nuclear factor 4. *J Biol Chem* **273**: 30847-50 [PMID:9812974]
  71. Wisely GB, Miller AB, Davis RG, Thornquest AD, Johnson R, Spitzer T, Sefler A, Shearer B, Moore JT, Miller AB, Willson TM and Williams SP. (2002) Hepatocyte nuclear factor 4 is a transcription factor that constitutively binds fatty acids. *Structure* **10**: 1225-34 [PMID:12220494]
  72. Yamagata K, Furuta H, Oda N, Kaisaki PJ, Menzel S, Cox NJ, Fajans SS, Signorini S, Stoffel M and Bell GI. (1996) Mutations in the hepatocyte nuclear factor-4alpha gene in maturity-onset diabetes of the young (MODY1). *Nature* **384**: 458-60 [PMID:8945471]
  73. Yoon JC, Puigserver P, Chen G, Donovan J, Wu Z, Rhee J, Adelmant G, Stafford J, Kahn CR, Granner DK,

- Newgard CB and Spiegelman BM. (2001) Control of hepatic gluconeogenesis through the transcriptional coactivator PGC-1. *Nature* **413**: 131-8 [PMID:11557972]
74. Yoshida E, Aratani S, Itou H, Miyagishi M, Takiguchi M, Osumu T, Murakami K and Fukamizu A. (1997) Functional association between CBP and HNF4 in trans-activation. *Biochem Biophys Res Commun* **241**: 664-9 [PMID:9434765]
75. Yuan X, Ta TC, Lin M, Evans JR, Dong Y, Bolotin E, Sherman MA, Forman BM and Sladek FM. (2009) Identification of an endogenous ligand bound to a native orphan nuclear receptor. *PLoS ONE* **4**: e5609 [PMID:19440305]
76. Zhang W, Tsuchiya T and Yasukochi Y. (1999) Transitional change in interaction between HIF-1 and HNF-4 in response to hypoxia. *J Hum Genet* **44**: 293-9 [PMID:10496070]