CODEN [USA]: IAJPBB ISSN: 2349-7750

INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES

http://doi.org/10.5281/zenodo.3401784

Available online at: http://www.iajps.com ***Research Article***

THE REGULATION OF LIPID METABOLISM BY TARGETING OPIOID RECEPTORS IN NONALCOHOLIC FATTY LIVER DISEASE

[1]Dr Ahmad Talal Asif, [2]Dr Sheikh Muhammad Rehman Zia, [3]Zahid Hussain

[1]House Officer at Mayo Hospital Lahore., [2]House Officer at Shalamar Hospital Lahore, [3]Final Year MBBS Student at Shalamar Medical and Dental College Lahore.

Article Received: July 2019 **Accepted:** August 2019 **Published:** September 2019

Abstract:

Nonalcoholic greasy liver infection (NAFLD) is an outstanding hepatic ailment. The pathogenesis of NAFLD can be improved by the tweak of narcotic receptors to weaken hepatic lipid variations from the norm. It is without a past filled with liquor misuse, which shows a brokenness of the ordinary procedures of lipid blend and end in hepatocytes. Aggravation has been believed to be related with the development of nonalcoholic steato-hepatitis (NASH) and elevates the movement to hepatic fibrosis and liver cirrhosis. The recognizable proof of potential mixes by focusing on narcotic receptors in the improvement of NAFLD is promising. Narcotic receptors appear to be engaged with the guideline of lipid and vitality digestion. Narcotic receptors appear to be engaged with the guideline of lipid and vitality digestion.

Key words: *Nonalcoholic steatohepatitis; Opioid receptor; Hepatic steatosis; Inflammation; Endoplasmic reticulum.*

Corresponding author:

Dr. Ahmad Talal Asif,

House Officer at Mayo Hospital Lahore.

QR code

Please cite this article in press Ahmad Talal Asif et al., ***The Regulation of Lipid Metabolism by Targeting Opioid Receptors in Nonalcoholic Fatty Liver Disease.,*** *Indo Am. J. P. Sci, 2019; 06(09).*

INTRODUCTION:

NAFLD starts as lipid collection in the liver (hepatic steatosis), and irritation can incite the pathogenesis of nonalcoholic steato-hepatitis (NASH) that can advance to various degrees of hepatic fibrosis and hepatocellular carcinoma[2]. The brokenness of lipid digestion in the liver is related with NAFLD in light of the fact that the expanded collection of greasy testimony in the liver can start a progression of incendiary reactions and pathologic changes. The clinical finding and assessment of NAFLD can be analyzed dependent on physical examination, disease history, ultrasound examination and hepatic imaging[1]. The pathogenesis of hepatic steatosis is identified with ways of life, dietary propensities and natural factors[3]. Nonalcoholic greasy liver illness (NAFLD) has pulled in much consideration in the ongoing years. Furthermore, hereditary variables and polymorphisms likewise add to the development of hepatic steatosis[4]. The impact and instrument of narcotic receptors on the improvement of NAFLD are as yet hazy. Strangely, narcotic receptors and peptides have been thought to assume a basic job in the guideline of endocrine digestion and glucose homeostasis in the past studies[5-7]. Hence, the survey plans to outline how NAFLD is kept from further movement by focusing on narcotic receptors to regulate the lipid digestion.

THE ROLE OF LIPID METABOLISM WITH INFLAMMATION IN NON-ALCOHOLIC FATTY LIVER DISEASE:

Lipids comprise of numerous particles, for example, phospholipids, unsaturated fats, cholesterols, and triglycerides. The impedance of lipid digestion prompts intemperate lipid amassing and triggers provocative reactions. A few investigations have demonstrated that aggravation is associated with numerous metabolic illnesses, including diabetes, hypertension, and NAFLD. Hepatic lipid digestion contains unsaturated fat blend, lipoprotein amalgamation and lipid oxidation [8], which is controlled at the genomic levels by various administrative proteins, metabolic catalysts, interpretation factors and co-regulators, for example, unsaturated fat transport protein (FATP), sugar responsive component restricting protein (ChREBP), sterol administrative component restricting protein (SREBP), acetyl-CoA carboxylase (ACC), lipoprotein lipase (LPL), liver X receptor (LXR), farnesoid X receptor (FXR), and peroxisome proliferator-initiated receptor (PPAR) [9-11]. Fiery cytokines can lessen the affectability of metabolic tissues or organs for metabolic hormones by upsetting the sign transduction of glucose and lipid digestion. Aggravation exasperates cell digestion and capacity by means of the endoplasmic reticulum (ER) stress or oxidative pressure, which instigates metabolic infections by meddling with ordinary glucose and lipid metabolism [12-14]. Take type 2 diabetes for instance, more elevated amounts of incendiary cytokines [e.g., Interleukin-1 beta (IL1β), Interleukin-6 (IL-6), Interleukin-18 (IL-18), C-receptive protein (CRP)], tumor putrefaction factor (TNF)- α and low dimensions of adiponectin are intently connected with the acceptance of insulin resistance [15]. The brokenness of hepatic lipid digestion with aggravation affects the advancement of NAFLD. The debilitation of lipid digestion by means of provocative reaction has been accounted for in NAFLD, and lipo-toxicity-prompted hepatic damage is described by the nearness of fiery cells in NASH [16]. Although, no creature model can totally show hepatic pathophysiology of NAFLD or NASH in people, the analysts can choose the appropriate creature model for their examinations as indicated by their exploratory structure. For the investigation of hepatic lipid digestion, numerous creature models have been embraced for the examination of NAFLD or NASH, including three primary sorts of creature models: (1) Combined creature models of hereditary alteration and dietary variables [e.g., db/db mice sustained with MCD diet and PPAR-α invalid mice encouraged with MCD diet] (2) Genetic creature models [e.g., SREBP-1c transgenic mice, ob/ob mice, db/db mice and phosphatase and tensin homologue erased on chromosome 10 (PTEN) invalid mice]; (3) Nutritional/dietary creature models [e.g., methionine and choline insufficiency (MCD) diet, high fat eating regimen (HFD), fructose diet and atherogenic diet] [17].

THE EFFECT OF OPIOID RECEPTOR ON LIPID AND ENERGY METABOLISM:

The guideline of narcotic receptors on lipid and vitality digestion stays cloud. The guideline of narcotic receptors with narcotic agonists or adversaries can influence numerous phone and neuronal sign transductions. The endogenous narcotic peptides contain dynorphins, enkephalins, endorphins, endomorphins and nociceptin. Narcotic receptors have a place with inhibitory G protein-coupled receptors. All in all, narcotic receptors are characterized into three subtypes, including mu (μ)-narcotic receptors (MOR), kappa (κ)- narcotic receptors (KOR) and delta (δ)- narcotic receptors (DOR) [18]. Numerous examinations have detailed that narcotic receptors affect the guideline of glucose metabolism[19, 20]. The initiation of focal narcotic receptors by particular agonists can invigorate craving. Cholesterol adds to narcotic receptor flagging by means of two components; keeping up

the aggregate of lipid pontoon micro-domains and straightforwardly encouraging narcotic receptor signaling[21, 22]. Endogenous narcotic peptides to be specific enkephalin and β-endorphin are thought to tweak vitality utilization and body weight by means of focusing on MOR and DOR. Galanin-incited nourishing of HFD is explicitly regulated by MOR flagging pathway in satisfied condition, though, that is intervened by KOR in starvation. The incitement of hypothalamic MOR advances the inclination of HFD[23], and HFD likewise instigates fat collection by means of the higher articulation of MOR in the cerebrum proposing diminished arrival of endogenous μ-narcotic peptides [24-28]. Weight with expanded adiposity and hindered glucose resilience is safe in MOR lacking (MOR-/ -) mice sustained with HFD, which is related with the enactment of metabolic catalysts engaged with unsaturated fat oxidation in skeletal muscle[29]. The restraint of narcotic receptors by narcotic foes can improve HFD-prompted dyslipidemia. The inclusion of narcotic receptors assumes a basic job in lipid and vitality digestion. The long haul organization of narcotic receptor adversaries can stifle hunger and body weight gain in hereditary stout creature models or corpulent people. Besides, the enmity of narcotic receptors can likewise decrease fat amassing by the incitement of lipid usage and the restraint of vitality consumption [30-34].

THE REGULATION OF OPIOID RECEPTORS IN NON-ALCOHOLIC FATTY LIVER DISEASE:

A few investigations have demonstrated that narcotic receptors can be potential medication focuses in the improvement of liver infections. Narcotic sign transduction is up-regulated in patients with provocative liver sickness, and some narcotic like mixes apply immune-modulatory exercises to lessen irritation. As per the past report, the hepatic articulations of MOR and DOR yet not KOR were available in the rodent showing the conveyance distinction of narcotic receptor subtypes. Up until this point, the job of narcotic receptors in the improvement of NAFLD has not been explained [35-38]. The overexpression of KOR in sidelong hypothalamic territory (LHA) can instigate hepatic steatosis through parasympathetic sensory system to manage lipid digestion; however, quieting of KOR articulation can nullify hepatic steatosis. The initiation of MOR with fringe MOR agonist can counteract intense hepatic aggravation and cell demise prompted by hepatotoxin. The lessening of KOR articulation can diminish hepatic triglyceride blend in mice encouraged with high-vitality diet (HED). In corpulent patients with NAFLD, the expanded articulation of narcotic receptors inside gastric mucosa is identified with the acceptance of fiery cytokines recommending the impact of narcotic receptors on the pathogenesis of NAFLD[39-42]. Moreover, melanin-concentrating hormone (MCH) builds lipid collection by the initiation of MCH receptors through the parasympathetic sensory system, which advances the arrangement of hepatic steatosis[43]. Taken together, the barricade of narcotic receptors by hereditary quieting or substance rivals gives advantageous impacts to the debilitation of lipid digestion in NAFLD. The higher articulation of DOR in hepatocellular carcinoma (HCC) is related with the tumor movement, which can be lessened by the quieting of DOR. Mice lacking DOR by hereditary interruption can diminish hepatic lipid content through the higher articulation of fat triglyceride lipase (ATGL) and increment thermogenesis in dark colored fat tissue (BAT) engaged with the enactment of uncoupling protein 1 (UCP1), peroxisome proliferatoractivated receptor gamma coactivator-1 α (PGC1α), and fibroblast development factor 21 (FGF21)[44-46].

CONCLUSION:

It is reasoned that the advancement of mixes for focusing on narcotic receptors will be gainful for the clinical patients with NAFLD. The guideline of lipid digestion by focusing on narcotic receptors can improve NAFLD and lessen the movement to NASH and hepatic fibrosis.

REFERENCES:

1. Cobbold JF, Patel D, Taylor-Robinson SD. Assessment of inflammation and fibrosis in non-alcoholic fatty liver disease by imaging-based techniques. J Gastroenterol Hepatol 2012; 27: 1281-1292 [PMID: 22432836]; [DOI: 10.1111/j.1440-1746.2012.07127.x]
2. Machado MV, Cortez-Pinto H. Non-alcoholic fatty liver disease: what the clinician needs to know. World J Gastroenterol 2014; 20: 12956-12980 [PMID: 25278691]; [DOI: 10.3748/wjg.v20.i36.12956]
3. Satapathy SK, Sanyal AJ. Epidemiology and Natural History of Nonalcoholic Fatty Liver Disease. Semin Lliver Dis 2015; 35: 221-235 [PMID: 26378640]; [DOI: 10.1055/s-0035-1562943]
4. Severson TJ, Besur S, Bonkovsky HL. Genetic factors that affect nonalcoholic fatty liver disease: A systematic clinical review. World J Gastroenterol 2016; 22: 6742-6756 [PMID: 27547017]; [DOI: 10.3748/wjg.v22.i29.6742]
5. Wen T, Peng B, Pintar JE. The MOR-1 opioid receptor regulates glucose homeostasis by

modulating insulin secretion. Mol Endocrinol 2009; 23: 671-678 [PMID: 19221053]; [DOI: 10.1210/me.2008-0345]
6. Xia FZ, Lu YL, Chen Y, Gu T, Zhang HX, Yu J, Zhao LJ. Peripheral endomorphin-1 levels are suppressed in diabetic patients. Diabetes Res Clin Pract 2010; 87: 200-203 [PMID: 20022398]; [DOI: 10.1016/j.diabres.2009.11.017]
7. Pfeiffer A, Herz A. Endocrine actions of opioids. Horm Metab Res 1984; 16: 386-397 [PMID: 6088380]; [DOI: 10.1055/s-2007-1014801]
8. Nguyen P, Leray V, Diez M, Serisier S, Le Bloc'h J, Siliart B, Dumon H. Liver lipid metabolism. J Anim Physiol Anim Nutr 2008; 92: 272-283 [PMID: 18477307]; [DOI: 10.1111/j.1439-0396.2007.00752.x]
9. Rui L. Energy metabolism in the liver. Compr Physiol 2014; 4: 177-197 [PMID: 24692138]; [DOI: 10.1002/cphy.c130024]
10. Katsiki N, Mikhailidis DP, Mantzoros CS. Non-alcoholic fatty liver disease and dyslipidemia: An update. Metabolism 2016; 65: 1109-1123 [PMID: 27237577]; [DOI: 10.1016/j.metabol.2016.05.003]
11. Cooke AA, Connaughton RM, Lyons CL, McMorrow AM, Roche HM. Fatty acids and chronic low grade inflammation associated with obesity and the metabolic syndrome. Eur J Pharmacol 2016; 785: 207-214 [PMID: 27083551]; [DOI: 10.1016/j.ejphar.2016.04.021]
12. Bozaykut P, Sahin A, Karademir B, Ozer NK. Endoplasmic reticulum stress related molecular mechanisms in nonalcoholic steatohepatitis. Mech Ageing Dev 2016; 157: 17-29 [PMID: 27393639]; [DOI: 10.1016/j.mad.2016.07.001]
13. Rutkowski DT, Wu J, Back SH, Callaghan MU, Ferris SP, Iqbal J, Clark R, Miao H, Hassler JR, Fornek J, Katze MG, Hussain MM, Song B, Swathirajan J, Wang J, Yau GD, Kaufman RJ. UPR pathways combine to prevent hepatic steatosis caused by ER stress-mediated suppression of transcriptional master regulators. Dev Cell 2008; 15: 829-840 [PMID: 19081072]; [DOI: 10.1016/j.devcel.2008.10.015]
14. Kratz M, Coats BR, Hisert KB, Hagman D, Mutskov V, Peris E, Schoenfelt KQ, Kuzma JN, Larson I, Billing PS, Landerholm RW, Crouthamel M, Gozal D, Hwang S, Singh PK, Becker L. Metabolic dysfunction drives a mechanistically distinct proinflammatory phenotype in adipose tissue macrophages. Cell Metab 2014; 20: 614-625 [PMID: 25242226]; [DOI: 10.1016/j.cmet.2014.08.010]
15. Liu C, Feng X, Li Q, Wang Y, Hua M. Adiponectin, TNF-alpha and inflammatory cytokines and risk of type 2 diabetes: A systematic review and meta-analysis. Cytokine 2016; 86: 100-109 [PMID: 27498215]; [DOI: 10.1016/j.cyto.2016.06.028]
16. Erikci Ertunc M, Hotamisligil GS. Lipid signaling and lipotoxicity in metabolic inflammation: indications for metabolic disease pathogenesis and treatment. J Lipid Res 2016 [PMID: 27330055]; [DOI: 10.1194/jlr.R066514]
17. Takahashi Y, Soejima Y, Fukusato T. Animal models of nonalcoholic fatty liver disease/nonalcoholic steatohepatitis. World J Gastroenterol 2012; 18: 2300-2308 [PMID: 22654421]; [DOI: 10.3748/wjg.v18.i19.2300]
18. Chung HH. The novel role of opioid μ-receptors in gastroenterology. J Gastroenterol Hepatol Res 2013; 2: 614-617 DOI: 10.6051/j.issn.2224-3992.2013.02.212]
19. Shang Y, Guo F, Li J, Fan R, Ma X, Wang Y, Feng N, Yin Y, Jia M, Zhang S, Zhou J, Wang H, Pei J. Activation of kappa-opioid receptor exerts the glucose-homeostatic effect in streptozotocin-induced diabetic mice. J Cell Biochem 2015; 116: 252-259 [PMID: 25186835]; [DOI: 10.1002/jcb.24962]
20. Gallagher CJ, Gordon CJ, Langefeld CD, Mychaleckyj JC, Freedman BI, Rich SS, Bowden DW, Sale MM. Association of the mu-opioid receptor gene with type 2 diabetes mellitus in an African American population. Mol Genet Metab 2006; 87: 54-60 [PMID: 16140553]; [DOI: 10.1016/j.ymgme.2005.07.013]
21. Zheng H, Zou H, Liu X, Chu J, Zhou Y, Loh HH, Law PY. Cholesterol level influences opioid signaling in cell models and analgesia in mice and humans. J Lipid Res 2012; 53: 1153-1162 [PMID: 22377533]; [DOI: 10.1194/jlr.M024455]
22. Gosnell BA, Levine AS, Morley JE. The stimulation of food intake by selective agonists of mu, kappa and delta opioid receptors. Life Sci 1986; 38: 1081-1088 [PMID: 2870405]
23. Barnes MJ, Holmes G, Primeaux SD, York DA, Bray GA. Increased expression of mu opioid receptors in animals susceptible to diet-induced obesity. Peptides 2006; 27: 3292-3298 [PMID: 16996647]; [DOI: 10.1016/j.peptides.2006.08.008]
24. Smith SL, Harrold JA, Williams G. Diet-induced obesity increases mu opioid receptor binding in specific regions of the rat brain. Brain Res 2002; 953: 215-222 [PMID: 12384255]
25. Barnes MJ, Lapanowski K, Conley A, Rafols JA, Jen KL, Dunbar JC. High fat feeding is associated with increased blood pressure, sympathetic nerve activity and hypothalamic mu

opioid receptors. Brain Res Bull 2003; 61: 511-519 [PMID: 13679250]
26. Barton C, York DA, Bray GA. Opioid receptor subtype control of galanin-induced feeding. Peptides 1996; 17: 237-240 [PMID: 8801527]
27. Mendez IA, Ostlund SB, Maidment NT, Murphy NP. Involvement of Endogenous Enkephalins and beta-Endorphin in Feeding and Diet-Induced Obesity. Neuropsychopharmacology 2015; 40: 2103-2112 [PMID: 25754760]; [DOI: 10.1038/npp.2015.67]
28. Reid LD. Endogenous opioid peptides and regulation of drinking and feeding. Am J Clin Nutr 1985; 42: 1099-1132 [PMID: 2865892]
29. Tabarin A, Diz-Chaves Y, Carmona Mdel C, Catargi B, Zorrilla EP, Roberts AJ, Coscina DV, Rousset S, Redonnet A, Parker GC, Inoue K, Ricquier D, Penicaud L, Kieffer BL, Koob GF. Resistance to diet-induced obesity in mu-opioid receptor-deficient mice: evidence for a "thrifty gene". Diabetes 2005; 54: 3510-3516 [PMID: 16306369]
30. Shaw WN. Long-term treatment of obese Zucker rats with LY255582 and other appetite suppressants. Pharmacol Biochem Behav 1993; 46: 653-659 [PMID: 8278442]
31. Atkinson RL. Naloxone decreases food intake in obese humans. J Clin Endocrinol Metab 1982; 55: 196-198 [PMID: 7042740]; [DOI: 10.1210/jcem-55-1-196]
32. Ibrahim IY, Ibrahim HM, Aziz NM, Rahman DM. The protective role of the opioid antagonist LY255582 in the management of high fat diet-induced obesity in adult male albino rats. Endocr Regul 2015; 49: 198-205 [PMID: 26494038]
33. Statnick MA, Tinsley FC, Eastwood BJ, Suter TM, Mitch CH, Heiman ML. Peptides that regulate food intake: antagonism of opioid receptors reduces body fat in obese rats by decreasing food intake and stimulating lipid utilization. Am J Physiol Regul Integr Comp Physiol 2003; 284: R1399-1408 [PMID: 12736177]; [DOI: 10.1152/ajpregu.00632.2002]
34. Shaw WN, Mitch CH, Leander JD, Mendelsohn LG, Zimmerman DM. The effect of the opioid antagonist LY255582 on body weight of the obese Zucker rat. Int J Obes 1991; 15: 387-395 [PMID: 1653188]
35. Wittert G, Hope P, Pyle D. Tissue distribution of opioid receptor gene expression in the rat. Biochem Biophys Res Commun 1996; 218: 877-881 [PMID: 8579608]; [DOI: 10.1006/bbrc.1996.0156]
36. Kiani S, Ebrahimkhani MR, Shariftabrizi A, Doratotaj B, Payabvash S, Riazi K, Dehghani M, Honar H, Karoon A, Amanlou M, Tavangar SM, Dehpour AR. Opioid system blockade decreases collagenase activity and improves liver injury in a rat model of cholestasis. J Gastroenterol Hepatol 2007; 22: 406-413 [PMID: 17295775]; [DOI: 10.1111/j.1440-1746.2006.04260.x]
37. Jaume M, Jacquet S, Cavailles P, Mace G, Stephan L, Blanpied C, Demur C, Brousset P, Dietrich G. Opioid receptor blockade reduces Fas-induced hepatitis in mice. *Hepatology* 2004; **40**: 1136-1143 [PMID: 15389866]; [DOI: 10.1002/hep.20428]
38. Day SA, Lakner AM, Moore CC, Yen MH, Clemens MG, Wu ES, Schrum LW. Opioid-like compound exerts anti-fibrotic activity via decreased hepatic stellate cell activation and inflammation. *Biochem Pharmacol* 2011; **81**: 996-1003 [PMID: 21291870]; [DOI: 10.1016/j.bcp.2011.01.015]
39. Mehta R, Birerdinc A, Wang L, Younoszai Z, Moazzez A, Elariny H, Goodman Z, Chandhoke V, Baranova A, Younossi ZM. Expression of energy metabolism related genes in the gastric tissue of obese individuals with non-alcoholic fatty liver disease. *BMC Gastroenterol* 2014; **14**: 72 [PMID: 24716593]; [DOI: 10.1186/1471-230X-14-72]
40. Chakass D, Philippe D, Erdual E, Dharancy S, Malapel M, Dubuquoy C, Thuru X, Gay J, Gaveriaux-Ruff C, Dubus P, Mathurin P, Kieffer BL, Desreumaux P, Chamaillard M. micro-Opioid receptor activation prevents acute hepatic inflammation and cell death. Gut 2007; 56: 974-981 [PMID: 17299060]; [DOI: 10.1136/gut.2006.105122]
41. Imbernon M, Sanchez-Rebordelo E, Romero-Pico A, Kallo I, Chee MJ, Porteiro B, Al-Massadi O, Contreras C, Ferno J, Senra A, Gallego R, Folgueira C, Seoane LM, van Gestel M, Adan RA, Liposits Z, Dieguez C, Lopez M, Nogueiras R. Hypothalamic kappa opioid receptor mediates both diet-induced and melanin concentrating hormone-induced liver damage through inflammation and endoplasmic reticulum stress. Hepatology 2016; 64: 1086-1104 [PMID: 27387967]; [DOI: 10.1002/hep.28716]
42. Czyzyk TA, Nogueiras R, Lockwood JF, McKinzie JH, Coskun T, Pintar JE, Hammond C, Tschop MH, Statnick MA. kappa-Opioid receptors control the metabolic response to a high-energy diet in mice. FASEB J 2010; 24: 1151-1159 [PMID: 19917675]; [DOI: 10.1096/fj.09-143610]
43. Imbernon M, Beiroa D, Vazquez MJ, Morgan DA, Veyrat-Durebex C, Porteiro B, Diaz-Arteaga A, Senra A, Busquets S, Velasquez DA,

Al-Massadi O, Varela L, Gandara M, Lopez-Soriano FJ, Gallego R, Seoane LM, Argiles JM, Lopez M, Davis RJ, Sabio G, Rohner-Jeanrenaud F, Rahmouni K, Dieguez C, Nogueiras R. Central melanin-concentrating hormone influences liver and adipose metabolism via specific hypothalamic nuclei and efferent autonomic/JNK1 pathways. Gastroenterology 2013; 144: 636-649 e636 [PMID: 23142626]; [DOI: 10.1053/j.gastro.2012.10.051]

44. Czyzyk TA, Romero-Pico A, Pintar J, McKinzie JH, Tschop MH, Statnick MA, Nogueiras R. Mice lacking delta-opioid receptors resist the development of diet-induced obesity. FASEB J 2012; 26: 3483-3492 [PMID: 22593549]; [DOI: 10.1096/fj.12-208041]
45. Zechner R, Kienesberger PC, Haemmerle G, Zimmermann R, Lass A. Adipose triglyceride lipase and the lipolytic catabolism of cellular fat stores. J Lipid Res 2009; 50: 3-21 [PMID: 18952573]; [DOI: 10.1194/jlr.R800031-JLR200]
46. Tang B, Li Y, Yuan S, Tomlinson S, He S. Upregulation of the delta opioid receptor in liver cancer promotes liver cancer progression both in vitro and in vivo. Int J Oncol 2013; 43: 1281-1290 [PMID: 23903826]; [DOI: 10.3892/ijo.2013.2046]