



Review Article

A review of current knowledge: Role of diabetes, cancer and cytochrome P450

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ABSTRACT

Diabetes mellitus (DM) is condition which is associated with metabolic diseases and considered as life-threatening illnesses worldwide, characterized by sustained hyperglycemia. DM is linked with diabetes mellitus (especially type 2 diabetes mellitus) and carcinogenesis and biologically it is comprise with Hyperinsulinemia, hyperglycemia and fat-induced chronic inflammation in both diabetes mellitus and cancer. Organs such as pancreas, hepatic breast, endometrium, prostate and kidney are highly involved in the disorder, several medications are available on the market which decrease the risk and some of them raise the risk including metformin, a medication of choice for type 2 DM and its anti-neoplastic and tumor suppressant activities. Research has indicated that metformin shows great positive impact in various organs like breast, pancreas, liver, colon, ovaries and prostate tumors, Cytochromes P450s (CYPs) is the enzyme that catalyzes and aids in drug metabolism with its endogenous CYP substrates like eicosanoids, estradiol, arachidonic acids, cholesterol, vitamin D, and neurotransmitters. We review the role of CYPs in cancer of the renal and breast, and address their importance for atherosclerosis and type 2 diabetes mellitus.

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1. Introduction

Diabetes mellitus is prevalent diseases in the world. It is a category of diseases that are characterized by a sustained hyperglycemia caused by inappropriate function or reduced insulin secretion. Persistent hyperglycemia causes different organs (kidneys, heart, lungs, blood vessels or nerves) to be weakened and dysfunction. Furthermore, DM and carcinogenesis are closely related.¹⁻⁴ the risk of carcinogenesis in type 1 diabetes mellitus (T1DM) is less evident than in type 2 diabetes mellitus (T2DM), although the risk was also documented.⁵ T1DM is one of the causes that raises the risk of stomach, cervix, endometrium, squamous skin cancers and acute lymphatic leukaemia.^{5,6} It is also recognized that tumors are the world's second-largest cause of death. Since cancer incidence in diabetics is widely observed, it is possible factors connecting these 2 diseases. Maynard and Pearson first identified the link

between DM and carcinogenesis in 1910 because the prevalence of T2DM is substantially higher than T1DM, and the cancer association studies are mainly focused on T2DM. A consensus study on potential factors connecting diabetes and cancer was published in 2010 by the American Diabetes Association (ADA) and the American Cancer Society (ACS).⁷ the risk factors were classified into three group's 1.non-modifiable risk factors, 2. Modifiable risk factors, and 3. Biological links between diabetes and cancer. (Table 1)

1.1. The relation between Diabetes Mellitus and Cancers

Recently literature research studies found the correlation between tumors located in various organs and DM. The results of studies on the influence of DM on tumorigenesis in different organs remain inconsistent. Nevertheless, the majority of authors implied that DM promotes tumor growth. Such relationship was observed in pancreatic, liver,

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Table 1: Factors linking DM and cancer

| Factors linking DM and cancer | | |
|--|--|--|
| Modifiable risk factors | Non-modifiable risk factors | Biological links between DM and cancer |
| Overweight (BMI > 25 < 30) | Physical activity Alcohol consumption | Hyperinsulinemia Insulin resistance |
| Obesity (BMI > 30) Physical activity Alcohol consumption | Smoking Age (55–60 years or older) Sex (men-higher risk) Ethnicity/race (African Americans more susceptible than Caucasians) | Hyperglycemia Fat-induced chronic inflammation |
| Smoking | | |

breast, kidney, bladder, endometrial, colorectal and head and neck cancers. Inverse association between these 2 diseases was observed only in prostate cancer. Here we discuss the current knowledge of the relationship "Diabetes Mellitus and site-specific cancer" which attempts to pose the risk of oncogenesis in different organs (Table 2).

1.2. Correlation between Anti-diabetic Therapies and increase Risk of Oncogenesis

It is suggested that anti-diabetic therapies interfere with cellular growth, proliferation and metabolism, and subsequently influence on potential oncogenesis. The Hyperinsulinemia and hyperglycemia are risk factors for carcinogenesis, thus lowering insulin and glucose levels seems to be an important matter in prevention of carcinogenesis.⁸

Antidiabetic medications are likely to have different effects on cancer risk due to the various doses of insulin induce, While sulfonylureas and exogenous insulin enhance insulin level, metformin and thiazolidinediones (TZD) are able to reduce its concentration.⁸ Moreover, metformin and TZD may reduce insulin resistance.⁹ A retrospective cohort study in the UK suggested that monotherapy with metformin is involved in the lowest risk of carcinogenesis.

Sulfonylureas presented increased risk of developing cancer in comparison with nonusers.¹⁰ Another study suggested that anti-diabetic therapy does not modify the risk of cancer in patients with T2DM.⁹ Here we suggest the recent studies about the mechanisms of action of various anti-diabetic medications and their potential influence on oncogenesis. (Table 3).

1.3. Incretin-Based Drugs (GLP-1 agonists, DDP-4-i)

1.3.1. Alpha-glucosidase inhibitors

Glucagon-peptide 1 agonists (GLP-1 agonists, including exenatide and Liraglutide) act as an Incretin hormone that leads to increased insulin secretion and decreased glucagon secretion. Such medicines also slow gastrointestinal motility.¹¹ Dipeptidyl peptidase-four, inhibitors (DDP-four which include Sitagliptin, Vildagliptin, Saxagliptin, Linagliptin, and Alogliptin) increase GLP-1 levels by inhibiting the DDP-4 (also known as CD26) enzyme that degrades GLP-1. The GLP-1 agonist therapy has been known to induce carcinogenesis in rodent C-cells but similar effects of GLP-1 agonists on human thyroid C-

cells have not been elucidated possibly due to different doses of GPL-1 Rs in rodent and human cells (high in rodents and low in human cells).¹² GLP-1R activation in rodent C-cells causes both Diabetes Mellitus and cancer, which is the leading cause of death worldwide. Since studies show that T2DM promotes carcinogenesis, it is important to reduce modifiable risk factors for Diabetes Mellitus, particularly in patients with age, sex, race / ethnicity, genetic susceptibility which is non modifiable risk factor. Obesity is an important modifiable factor for T2DM as well as for cancer. Reducing weight decreases insulin resistance, Hyperinsulinemia and adiposity-related chronic inflammation (all of the aforementioned states are tumor-promoting mechanisms and increase risk of T2DM). Multiple studies established that Diabetes Mellitus increases the risk of occurrence of cancers in various organs and decreases the potential risk of prostate cancer incidence. Furthermore, the fact suggest that diabetics presently increased risk of different cancers incidence, the overall survival, they should develop cancer, is worse than in no diabetics (Table 4 & 5)

The cytochrome P450 (CYP) is a large superfamily of integral membrane conserved proteins present in animals, plants, and microorganisms.¹³ The CYP iso enzyme superfamily comprises 57 CYP genes and 58 pseudo genes arranged into 18 families and 43 subfamilies in man.¹⁴ they are heme-containing proteins that catalyze the oxidative metabolism of many structurally diverse drugs and chemicals. They are heme-containing proteins that catalyze the oxidative metabolism of many structurally diverse drugs and chemicals.¹⁵ The reduced cytochrome P450 iso enzymes when bound to CO has a Soret peak at 450 nm This peak is not usual for a hem containing protein molecule. Hence, they are called P450.¹⁶ the cytochrome P450 superfamily is located primarily in liver, small intestine and kidney.¹⁷ CYPs P450 enzymes catalyze different oxidation and some reduction reactions.¹⁸ Examples of the substrates.¹⁹ of CYPs include exogenous (xenobiotics) and endogenous compounds such as cholesterol, testosterone, progesterone, prostaglandin H2, corticosterone, retinoic acid vitamin D3 and arachidonic acid.²⁰

Table 2: Risk of oncogenesis in patients with DM

| Cancer | Risk of oncogenesis in patients with DM |
|------------------|--|
| Pancreatic | ↑↑ |
| Liver | ↑↑↑ |
| Breast | ↑↑ |
| Kidney | ↑ |
| Endometrial | ↑↑ |
| Colon/colorectal | ↑↑ |
| Bladder | ↑ |
| HNC | Larynx↑/no significance association/↓ Oral cavity ↑ Oropharynx ↑ Nasopharynx ↑ HNSCC ↓ |
| Prostate | ↓↓/↑ |

↓- decreased risk
 ↑- increased risk

Table 3: Anti-diabetic drugs, their Mechanism of action and risk of oncogenesis

| Medication | Mechanism of action | Risk of oncogenesis |
|--------------------------|--|--|
| Metformin | Systemic effects: ↓serum glucose level ↓hepatic gluconeogenesis and glycogenolysis ↓gastrointestinal absorption of glucose ↓insulin level Inhibited inflammatory response Cell intrinsic effects: ↓ATP level Activation of LKB1-AMPK pathway Inhibition of mTOR signaling Activation of p53, p21, cyclin D1 Inhibition of UPR Cell cycle arrest Apoptosis induction ↓ROS production ↓NADH utilization ↑CD8 T-cell production Destruction of cancer stem cells | Breast ↓ Pancreas ↓ Liver ↓ Colorectum ↓/↑ Prostate ↓ Lung ↓ Ovaries ↓ Kidney ↓ HNC ↓/no significant reduction |
| Sulfonylureas | Closing potassium channels ↑insulin secretion ↑fasting and postprandial insulin level | Gliclazide ↓ Glibenclamide ↑/↓ Colon ↑ Liver ↑ Prostate ↓ |
| Exogenous insulin | ↑ insulin concentration | Prostate ↓ Liver ↑ Pancreas ↑ Stomach ↑ Kidney ↑ Colon ↓/↑ (glargine) Breast↑ (glargine) Endometrium↑ (glargine) Prostate↑ (glargine) Neutral effect of glargine |
| α-glucosidase inhibitors | Delayed digestion of polysaccharides by inhibiting enzymes saccharase and maltase in proximal small intestine | Stomach ↓ Lungs ↓ Kidney ↑ |
| DDP-4-i | Inhibition of DDP-4 ↑level of GLP-1 | Pancreas ↑ Colon ↓ No tumor-promoting effect |
| GLP-1 agonists | ↑secretion of insulin ↓secretion of glucagon Delayed gastrointestinal motility Inhibition of PI3K/AKT pathway | Pancreas ↑/↓ ↓proliferation of prostate, colon and breast cancer cells ↑in rodent C-cells but not in human C-cells |
| TZD | Activation of PPAR, Suppression of Bcl-2/Bcl-xL function, Inhibition of androgen activation | Pancreas ↓ Breast ↓ Colorectum ↓ Lungs ↓ Kidney ↓ Liver ↓ Colon ↓ |

↓- decreased risk
 ↑- increased risk

Table 4: Cancers of digestive system and DM.

| | Increased risk in diabetics | Decreased risk in diabetics |
|-------------------------|-----------------------------|-----------------------------|
| Pancreatic cancer | ↑↑ | - |
| Liver cancer | ↑↑↑ | - |
| Colon/colorectal cancer | ↑ | - |

↓- decreased risk
 ↑- increased risk

Table 5: Cancers of genitourinary system and DM.

| | Increased risk in diabetics | Decreased risk in diabetics |
|--------------------|-----------------------------|-----------------------------|
| Bladder cancer | ↑↑ | - |
| Kidney cancer | ↑↑↑ | - |
| Endometrial cancer | ↑↑ | - |
| Prostate cancer | ↑ | ↓↓ |

↓- decreased risk

↑- increased risk

1.4. Role of Cytochrome P450 in Cancers

1.4.1. Renal cancer

It has been shown that the cytochrome P450 (CYP3A) types are reliably expressed in kidney cancer cells using immunohistochemistry, western blot analysis, and reverse transcriptase PCR. This research indicated that the CYP3A expressed could be involved in the development of renal cancer, and that these types of CYP3A are the source of the multidrug resistance found in this cancer. In addition, they indicated that the presence of CYP3A types in the renal cells would be useful for treating renal cancer. For instance, the agent AQ4N, an alkylaminoanthroquinone is bio activated by CYP3A forms to a highly cytotoxic metabolite in the hypoxic conditions of the tumor cells, but the AQ4N would not be cytotoxic for the normal cells where the conditions are normoxic.²¹ the cytochrome CYP1B1 was also shown to be present in renal cell carcinoma. It is also expressed in wide variety of cancers and not detected in normal cells.²²

It has been proposed that since CYP1B1 is the metabolizing enzyme for the anticancer drugs (e.g. cyclophosphamide, paclitaxel, doxorubicin, docetaxel, cisplatin, 5-fluorouracil) its inhibition may be a good strategy for cancer therapy.²³ Recently, it has been suggested CYP1B1 is significantly unregulated in renal cell carcinoma, and that it promotes this cancer progression.²⁴

1.4.2. Breast Cancer

It has been documented that CYP2E1 in breast cancer cells contributes to the production of the reactive oxygen species (ROS). Furthermore, CYP2E1 controls autophagy, induces the tension of endoplasmic reticulum, and suppresses the BC cells' metastatic potential. CYP2E1 expression shows to greatly increase in BC cells as well as tissues adjacent to the tumor. The overexpression of the CYP2E1 enzyme may be beneficial to the cancer patient this advantage comes from the activation property of CYP2E1 pro drugs and that the metabolism of some CYP2E1 substrates contributes to ROS development and oxidative stress. This will ultimately lead to apoptosis inhibition but will accelerate the death of the necrotic cancer cells. In a review the expression profile of CYP450 enzymes in (BC) in Caucasian population was studied. It has been confirmed that the CYP4X1, CYP2S1 and CYP2U1 regulations exist.²⁵

1.5. Roles of Cytochrome P450 in Diabetes

CYP2E1 oxidizes ethanol and stimulates procarcinogens such as N-nitrosodimethylamine, benzene and N-alkylformamides.²⁶ it has been shown that CYP2E1 is over-expressed in alcohol-induced liver damage and non-alcoholic steatosis.²⁷ Diabetes is generally associated with fat mobilization because it will be the first source of energy that will contribute to non-alcoholic production.²⁸

1.6. Roles of Cytochrome P450 in Atherosclerosis

Arachidonic acid is metabolized to epoxyeicosatrienoic acids (EETs) by CYP450 (CYP 2B, 2C8, 2C9, 2C10, 2J2), or arachidonic acid epoxygenase. The EETs function as a hyperpolarizing factor (EDHF) derived from endothelium that acts as a vasodilator in all vasculatures including the coronary arteries.²⁹ The EDHF metabolite of arachidonic acid by CYP2C has been shown to Hence, these CYP450 enzymes prevent or regress atherosclerosis.³²

1.7. Cytochrome P450 Gene Polymorphism

Genetic polymorphisms in CYPs are a major cause of the inter individuals variation in drug metabolism. They lead to the occurrence of variation in response to the drugs ranging from adverse effects to lack of efficacy.³³ From the 50 identified CYPs iso enzymes that catalyze the drug metabolism, there are more than 20 genes of CYPs are functionally polymorphic, for instance the CYP2A6, CYP2C9, CYP2C19, CYP2D6, CYP1B1, and CYP1A2. Therefore, about 40% of drug metabolism is catalyzed by the polymorphic CYPs.³⁴

2. Conclusion

The study indicated that both diabetes and cancer are linked to each other with modifiable risk factors, non-modifiable risk factors, and biological linkages between Diabetes Mellitus and cancer, these create the leading cause of death in both developing and developed countries and considered to be life-threatening diseases across the world globe. Persistent hyperglycemia causes different organs (kidneys, heart, lungs, blood vessels or nerves) to be weakened and dysfunction. Additionally, Diabetes Mellitus and carcinogenesis are closely related. The risk of carcinogenesis in type 1 diabetes mellitus (T1DM) is

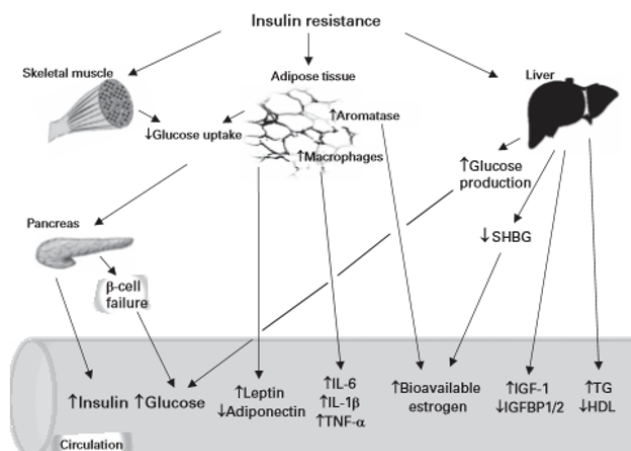


Fig. 1: Potential mechanisms linking diabetes and cancer

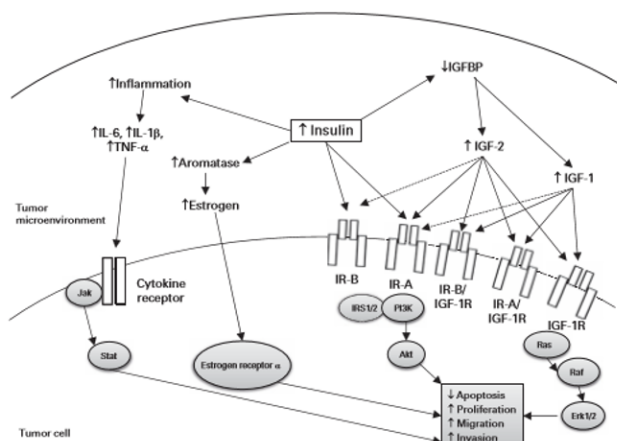


Fig. 2: T2DM and Cancer: Role of Pharmacotherapy

less apparent than in type 2 diabetes mellitus (T2DM). The T2DM is associated with an increased incidence and mortality from many cancers such as breast cancer, renal cancer. The use of metformin has been linked with a reduction in cancer incidence and mortality and several ongoing randomized trials examine the impact of metformin on cancer-related outcomes. The cytochrome p450 is the enzyme that enhances the various oxidation and reduction reaction and several other drug. These cytochrome p450 has shown its significant role in several cancers which include breast cancer, renal cancer. Mainly in breast cancer, the CYP2E1 has a great role for producing reactive oxygen species (ROS) and controlling autophagy, inducing endoplasmic reticulum tension and suppressing BC cell that provide the better anticancer activity in patients where, as in another associated cancer such as renal cancer, CYP3A4 form plays a great significant role which was identified by immunohistochemistry, western blot analysis, and reverse transcription PCR. Hence, provide the better treatment with their associated risk for the disease. The cytochrome p450

has also its role in various others which include diabetes, atherosclerosis, and gene polymorphism.

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5. Conflict of Interest

None.

References

- Giovannucci E, Harlan DM, Archer MC, Bergenstal RM, Gapstur SM, Habel LA, et al. Diabetes and Cancer: A consensus report. *Diabetes Care*. 2010;33(7):1674–85.
- Jee SH, Ohrr H, Sull JW. Fasting serum glucose level and cancer risk in Korean men and women. *JAMA*. 2005;293:194–202.
- Tseng KS, Lin C, Lin YS. Risk of head and neck cancer in patients with diabetes mellitus: a retrospective cohort study in Taiwan. *JAMA Otolaryngol Head Neck Surg*. 2014;140:746–53.
- Noto H, Tsujimoto T, Sasazuki T, Noda M. Significantly Increased Risk of Cancer in Patients with Diabetes Mellitus: A Systematic Review and Meta-Analysis. *Endocr Pract*. 2011;17(4):616–28.
- Zendehdel K. Cancer Incidence in Patients With Type 1 Diabetes Mellitus: A Population-Based Cohort Study in Sweden. *Cancer Spectr Knowledge Environ*. 2003;95(23):1797–1800.
- Shu X, Ji J, Li X, Sundquist J, Sundquist K, Hemminki K, et al. Cancer risk among patients hospitalized for Type 1 diabetes mellitus: a population-based cohort study in Sweden. *Diabetic Med*. 2010;27(7):791–7.
- Gallagher EJ, LeRoith D. Diabetes, cancer, and metformin: connections of metabolism and cell proliferation. *Ann N York Acad Sci*. 2011;1243(1):54–68.
- Onitilo AA, Engel JM, Glurich I, Stankowski RV, Williams GM, Doi SA, et al. Diabetes and cancer II: role of diabetes medications and influence of shared risk factors. *Cancer Causes Control*. 2012;23(7):991–1008.
- Simó R, Plana-Ripoll O, Puente D, Morros R, Mundet X, Vilca LM, et al. Impact of Glucose-Lowering Agents on the Risk of Cancer in Type 2 Diabetic Patients. The Barcelona Case-Control Study. *PLoS ONE*. 2013;8(11):e79968.
- Currie CJ, Poole CD, Gale EAM. The influence of glucose-lowering therapies on cancer risk in type 2 diabetes. *Diabetologia*. 2009;52(9):1766–77.
- Nathan DM, Buse JB, Davidson MB, Ferrannini E, Holman RR, Sherwin R, et al. Medical Management of Hyperglycemia in Type 2 Diabetes: A Consensus Algorithm for the Initiation and Adjustment of Therapy: A consensus statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care*. 2009;32(1):193–203.
- Samson SL, Garber A. GLP-1R agonist therapy for diabetes. *Curr Opin Endocrinol Diabetes Obesity*. 2013;20(2):87–97.

13. Nebert DW, Russell DW. Clinical importance of the cytochromes P450. *Lancet*. 2002;360(9340):1155–62.
14. Nelson DR, Zeldin DC, Hoffman SM, Maltais LJ, Wain HM, Nebert DW, et al. Comparison of cytochrome P450 (CYP) genes from the mouse and human genomes, including nomenclature recommendations for genes, pseudogenes and alternative-splice variants. *Pharmacogenetics*. 2004;14(1):1–18.
15. Womack CJ, Saunders MJ, Bechtel MK, Bolton DJ, Martin M, Luden ND, et al. The influence of a CYP1A2 polymorphism on the ergogenic effects of caffeine. *J Int Soc Sports Nutr*. 2012;9(1):1–7.
16. Luthra A, Denisov IG, Sligar SG. Spectroscopic features of cytochrome P450 reaction intermediates. *Arch Biochem Biophys*. 2011;507(1):26–35.
17. Thelen K, Dressman JB. Cytochrome P450-mediated metabolism in the human gut wall. *J Pharm Pharmacol*. 2009;61:541–8.
18. Guengerich FP. Mechanisms of cytochrome P450 substrate oxidation: MiniReview. *J Biochem Mol Toxicol*. 2007;21(4):163–8.
19. Porter TD, Coon MJ. Cytochrome P-450. Multiplicity of isoforms, substrates, and catalytic and regulatory mechanisms. *J Biol Chem*. 1991;266:13469–72.
20. Guengerich FP. Intersection of the Roles of Cytochrome P450 Enzymes with Xenobiotic and Endogenous Substrates: Relevance to Toxicity and Drug Interactions. *Chem Res Toxicol*. 2017;30(1):2–12.
21. Murray GI, McFadyen MCE, Mitchell RT, Cheung YL, Kerr AC, Melvin WT, et al. Cytochrome P450 CYP3A in human renal cell cancer. *Br J Cancer*. 1999;79(11-12):1836–42.
22. McFadyen MCE, Melvin WT, Murray GI. Cytochrome P450 CYP1B1 activity in renal cell carcinoma. *Br J Cancer*. 2004;91(5):966–71.
23. Mcfadyen MC, Mcleod HL, Jackson FC. Cytochrome P450 CYP1B1 protein expression: a novel mechanism of anticancer drug resistance. *Biochem Pharmacol*. 2001;62:207–12.
24. Mitsui Y, Chang I, Fukuhara S. CYP1B1 promotes tumorigenesis via altered expression of CDC20 and DAPK1 genes in renal cell carcinoma. *BMC Cancer*. 2015;15:942.
25. Vaclavikova R, Hubackova M, Stribrna-Sarmanova J. RNA expression of cytochrome P450 in breast cancer patients. *Anticancer Res*. 2007;27:4443–50.
26. Wang Z, Hall SD, Maya JF, Li L, Asghar A, Gorski JC, et al. Diabetes mellitus increases the in vivo activity of cytochrome P450 2E1 in humans. *Br J Clin Pharm*. 2003;55(1):77–85.
27. Niemelä O, Parkkila S, Juvonen RO, Viitala K, Gelboin HV, Pasanen M, et al. Cytochromes P450 2A6, 2E1, and 3A and production of protein-aldehyde adducts in the liver of patients with alcoholic and non-alcoholic liver diseases. *J Hepatol*. 2000;33(6):893–901.
28. Hazlehurst JM, Woods C, Marjot T, Cobbold JF, Tomlinson JW. Non-alcoholic fatty liver disease and diabetes. *Metab*. 2016;65(8):1096–1108.
29. Chawengsub Y, Gauthier KM, Campbell WB. Role of arachidonic acid lipoxygenase metabolites in the regulation of vascular tone. *Am J Physiol-Heart and Circ Physiol*. 2009;297(2):495–507.
30. Fisslthaler B, Fleming I, Busse R. a cytochrome P450 metabolite in coronary arteries. *Semin Perinatol*. 2000;24:15–9.
31. Chawengsub Y, Gauthier KM, Campbell WB. Role of arachidonic acid lipoxygenase metabolites in the regulation of vascular tone. *Am J Physiol-Heart Circ Physiol*. 2009;297(2):495–507.
32. Luoma PV. Cytochrome P450 — physiological key factor against cholesterol accumulation and the atherosclerotic vascular process. *Ann Med*. 2007;39(5):359–70.
33. Sim SC, Ingelman-Sundberg M. The Human Cytochrome P450 (CYP) Allele Nomenclature website: a peer-reviewed database of CYP variants and their associated effects. *Human Genomics*. 2010;4(4):278–81.
34. Bernard S, Neville KA, Nguyen AT, Flockhart DA. Interethnic Differences in Genetic Polymorphisms of CYP2D6 in the U.S. Population: Clinical Implications. *Oncol*. 2006;11(2):126–35.

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