

Preprint 47: Tretinoin Numerical and Structural Similarities for Expression Modification in Retinol Metabolism

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1 Abstract

Dermatologicals such as (1) Prenol lipids, (2) Isoprenoids and (3) Retinoids are involved in used in the treatment of acne with the compound Tretinoin. Tretinoin Similarities (e.g. C₂₀H₂₈O₂) were examined in Retinol metabolism and the Retinoic acid receptor (RAR) and retinoid X receptor (RXR) agonists/antagonists in Th17 cell differentiation, Pathways in cancer, Transcriptional misregulation in cancer and Acute myeloid leukemia, both small and non small cell lung cancer, and gastric cancer. Here the chemical reactions of retinol is examined with products with Tretinoin Similarities. No significant correlation was found in the NCI-60 expressions with puromycin for genes BAG4, BAG1, CYP1A2, RARA, BAG3, TP53, and TP73.

2 Introduction

Hemoprotein reductase (Oxidized flavoprotein) is a group of P-450 heme-thiolate proteins that act on a wide range of substrates including many xenobiotics, steroids, fatty acids, vitamins and prostaglandins; reactions catalysed include hydroxylation, epoxidation, N-oxidation, sulfoxidation, N-, S- and O-dealkylations, desulfation, deamination, and reduction of azo, nitro and N-oxide groups. [400]

Together with EC 1.6.2.4, NADPH—hemoprotein reductase, it forms a system in which two reducing equivalents are supplied by NADPH. Some of the reactions attributed to EC 1.14.15.3, alkane 1-monooxygenase.

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Acting on paired donors, with incorporation or reduction of molecular oxygen; With reduced flavin or flavoprotein as one donor, and incorporation of one atom of oxygen into the other donor. . [400]

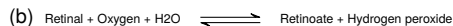
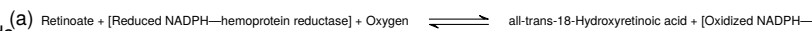
NADPH has a role in (a) cytochrome P450 mono-oxygenase, (b) reduction of glutathione, (c) reduction biosynthesis, (d) role in cell, (e) role in phagocytosis by white blood cells, (f) role in red blood cells, (g) source in fatty acid synthesis, (h) steroid hormone synthesis, and (i) thioredoxin reductase. Here NADPH like NADH is a high energy molecule and present in the stoichiometry of the citric acid cycle with



Nuclear receptors such as Thyroid hormone like receptors like Retinoic acid receptor (RAR) are affected by Tretinoin with examples in the following pathways [400]

1. map00830 Retinol metabolism
2. map01100 Metabolic pathways
3. map04659 Th17 cell differentiation
4. map04672 Intestinal immune network for IgA production
5. map05200 Pathways in cancer
6. map05222 Small cell lung cancer
7. map05223 Non-small cell lung cancer
8. map05226 Gastric cancer

The enzymes involved are: 1.2.1.36, 1.2.3.1, 1.14.14.1, 1.14.14.- and 2.4.1.17 are involved. Lipids such as Prenol lipids, Isoprenoids include Retinoids such as Retinoate Retinoate, Retinoic acid, Vitamin A acid with Formula C₂₀H₂₈O₂, Exact mass 300.2089 and Mol weight 300.4351. Retinoids for cancer treatment include Tretinoin that is an Dermatological Agents for Acne and Rosacea Agents that affect cellular function and Antitumors with a SMILE Notation CC1=C(C(CCC1)(C)C)C=CC(=CC=CC(=CC(=O)O)C)C. [401] Reactions include:



for CYP1A1, CYP2A6, CYP2B6, CYP2C8/9/18, CYP3A4/5/7, CYP26, CYP4A11 The pathways involved for CYP1A2 Expression are:

1. hsa00140 Steroid hormone biosynthesis
2. hsa00232 Caffeine metabolism
3. hsa00380 Tryptophan metabolism
4. hsa00591 Linoleic acid metabolism
5. hsa00830 Retinol metabolism
6. hsa00980 Metabolism of xenobiotics by cytochrome P450
7. hsa00982 Drug metabolism - cytochrome P450
8. hsa01100 Metabolic pathways
9. hsa05204 Chemical carcinogenesis

Figure One has Retinol metabolism.

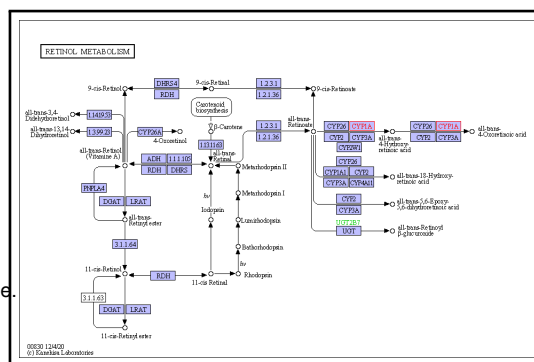


Figure 1: Retinol in Vitamin Absorption Digestion and Enzymes 1.1.1.1, 1.1.1.105, 1.1.1.300, 1.1.1.1., 1.3.99.23, 1.14.19.53, 2.3.1.76, 2.3.1.135 and 3.1.1.-

Figure Two has the map of Chemical carcinogenesis.

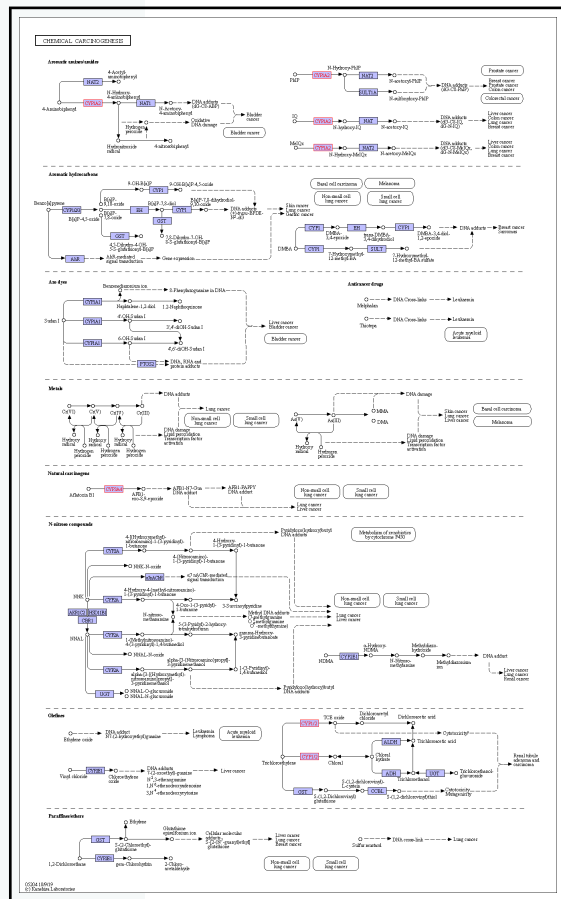


Figure 2: Chemical carcinogenesis

3 Results

In this article, the pathways of Retinol was examined with CYP1A2 and Chemical carcinogenesis. Tretinoin (JAN/USP/INN); Avita (TN); Renova (TN); Retin A (TN); and Tretinoin (TN) has molecular formula C₂₀H₂₈O₂ with Exact mass of 300.2089 Mol weight 300.4351 and Pathways include Th17 cell differentiation, Pathways in cancer, Transcriptional misregulation in cancer and Acute myeloid leukemia. Figure 3 has Retinoic acid receptor (RAR) and retinoid X receptor (RXR) agonists/antagonists.

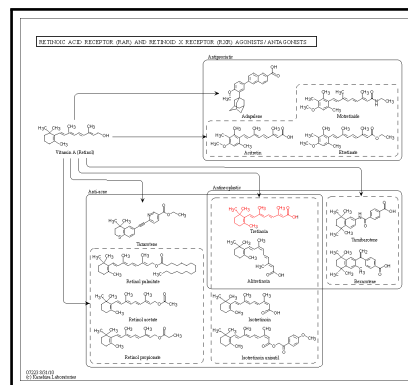


Figure 3: Retinoic acid receptor (RAR) and retinoid X receptor (RXR) agonists/antagonists

3.1. Tretinoin Similarities

Figure 4 has the Atom Frequencies for the Similarity Collection based on CC1=C(C(CCC1)(C)C)C=CC(=CC=CC(=CC(=O)O)C)C with Tanimoto Index=0.8. [470]

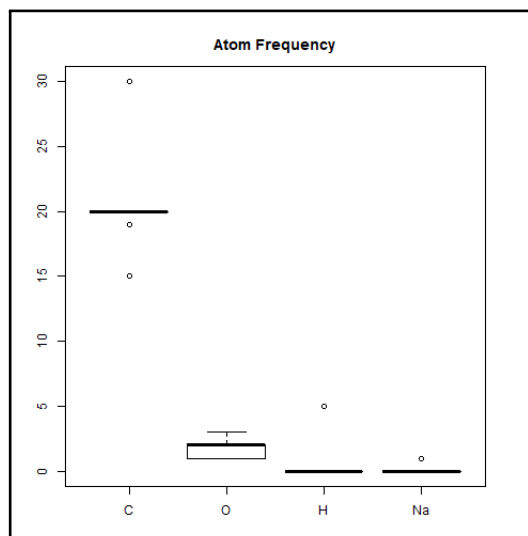


Figure 4: Atom Frequency

Table One has C, O, H and N amounts. [701]

	C	O	H	Na
CMP1	20.00	2.00	0.00	0.00
CMP2	20.00	2.00	0.00	0.00
CMP3	20.00	2.00	0.00	0.00
CMP4	20.00	2.00	5.00	0.00
CMP5	20.00	2.00	5.00	0.00
CMP6	20.00	2.00	0.00	1.00
CMP7	15.00	2.00	0.00	0.00
CMP8	30.00	1.00	0.00	0.00
CMP9	20.00	1.00	0.00	0.00
CMP10	20.00	1.00	0.00	0.00
CMP11	20.00	1.00	0.00	0.00
CMP12	20.00	1.00	0.00	0.00
CMP13	20.00	1.00	0.00	0.00
CMP14	19.00	2.00	0.00	0.00
CMP15	20.00	3.00	0.00	0.00

Table 2 has the name, chemical formulas and mass for some example similarities. [470]

Name	Formula	Mass
4-amino-3-pentadecylphenol	C ₂₁ H ₃₇ NO	319.287514804
tris(4-biphenyl)methanol	C ₃₇ H ₂₈ O	488.214015516
thymophthalein	C ₂₈ H ₃₀ O ₄	430.21440944
Actinomycin D	C ₆₂ H ₈₆ N ₁₂ O ₁₆	1254.628474672
puromycin	C ₂₂ H ₂₉ ClN ₇ O ₅	506.191869708
badil	C ₂₅ H ₃₀ ClN ₃	407.21282564
methyl green	C ₂₇ H ₃₅ BrClN ₃	515.1702879
crude pyronine b	C ₂₁ H ₃₁ Cl ₄ FeN ₂ O	523.053986832
wln: t6nj c- bl5ktj a1 a2- at5ktj a1 b- ct6njg 2i 2	C ₂₂ H ₃₂ N ₄	352.262697024
quinacrine mustard	C ₂₃ H ₂₈ Cl ₄ N ₃ O	502.098648236
urson	C ₃₀ H ₄₈ O ₃	456.360345396

Table 3 has the results for puromycin with the genes BAG4, BAG1, CYP1A2, RARA, BAG3, TP53, and TP73 expressions from the NCI-60 cell lines. [1006]

	COR	PVAL	QVAL
BAG4	0.27	0.06	0.45
BAG1	0.22	0.13	0.46
CYP1A2	0.18	0.24	0.56
RARA	-0.12	0.41	0.58
BAG3	-0.12	0.41	0.58
TP53	0.01	0.95	0.95
TP73	-0.01	0.94	0.95

Figures Five, Six, Seven and Eight has the Tretinoin Similarites of the Tanimoto 0.8. [470]

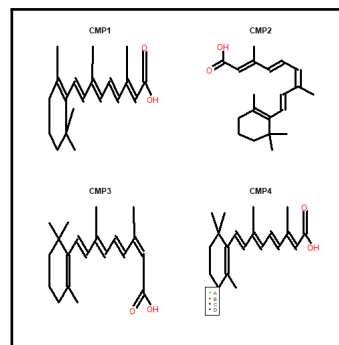


Figure 5: Tretinoin Similarites Tanimoto 0.8 [701]

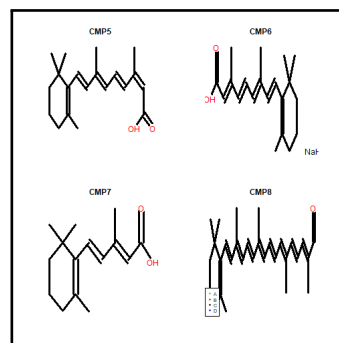


Figure 6: Tretinoin Similarites Tanimoto 0.8 [701]

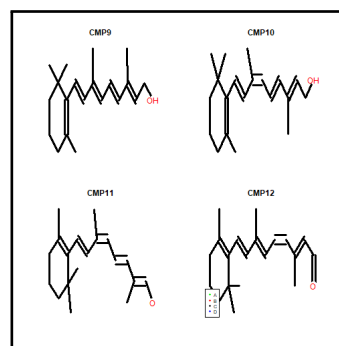


Figure 7: Tretinoin Similarites Tanimoto 0.8 [701]

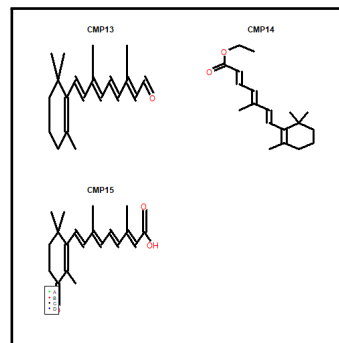


Figure 8: Tretinoin Similarites Tanimoto 0.8 [701]

4 Conclusion

In this mathematical biology article, Retinoin Similarites were examined in Retinol metabolism and the Retinoic acid receptor (RAR) and retinoid X receptor (RXR) agonists/antagonists in Th17 cell differentiation, Pathways in cancer, Transcriptional misregulation in cancer and Acute myeloid leukemia. Here Retinoate [Reduced NADPH—hemoprotein reductase] Oxygen, all-trans-18-Hydroxyretinoic acid [Oxidized NADPH—hemoprotein reductase] H₂O, Retinal and Hydrogen peroxide (H₂O₂) are involved along with CYP1A1, CYP2A6, CYP2B6, CYP2C8/9/18, CYP3A4/5/7, CYP26, CYP4A11. No significant correlation was found in the NCI-60 expressions with puromycin for genes BAG4, BAG1, CYP1A2, RARA, BAG3, TP53, and TP73.

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