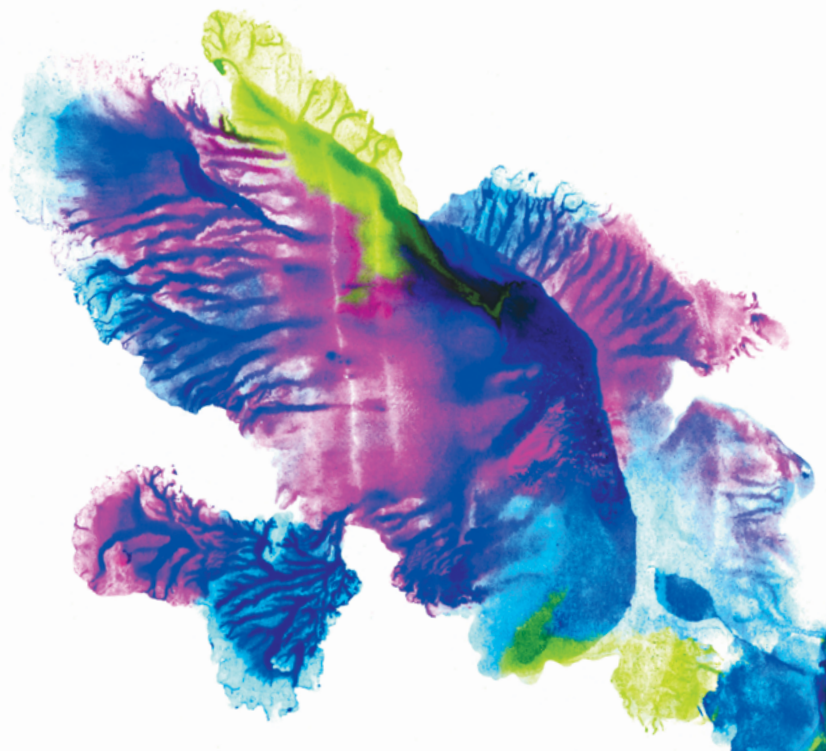




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STEROIDOGENESIS PATHWAYS REFERENCES

1. Cholesterol Activation: (StAR and CYP11A1)

- Lee, H., et al., "Retinoic acids up-regulate steroidogenic acute regulatory protein gene", *Molecular & Cellular Endocrinology*, vol. 148, no. 1-2, February 1999, pp. 1-10, DOI: 10.1016/s0303-7207(98)00243-3
- **Manna, P.R.**, et al. "Synergistic Activation of Steroidogenic Acute Regulatory Protein Expression and Steroid Biosynthesis by Retinoids: Involvement of cAMP/PKA Signaling", *Endocrinology*. Vol. 155, no. 2, 2014, pp. 576-591, doi: 10.1210/en.2013-1694
- **Mast, N.** et al. "Inhibition and stimulation of activity of purified recombinant CYP11A1 by therapeutic agents", *Molecular & Cellular Endocrinology*, vol. 371, no. 1-2, May 2013, pp. 100-6, doi: 10.1016/j.mce.2012.10.013.

2. CYP17A (17 α -hydroxylase)

- **Bird, I.M.** and Abbott, D.H. "The hunt for a selective 17,20 lyase inhibitor; learning lessons from nature", *Journal of Steroid Biochemistry & Molecular Biology*, vol.163, October 2016, pp. 136-46, doi: 10.1016/j.jsbmb.2016.04.021.
- **Malikova, J.L.**, et al., "CYP17A1 inhibitor abiraterone, an anti-prostate cancer drug, also inhibits the 21-hydroxylase activity of CYP21A2", *Journal of Steroid Biochemistry and Molecular Biology*, vol. 174, November 2017, pp. 192-200. doi: 10.1016/j.jsbmb.2017.09.007. Epub 2017 Sep 8.
- **Nelson-Degrave, V.L.**, et al., "Valproate Potentiates Androgen Biosynthesis in Human Ovarian Theca Cells", *Endocrinology*, vol. 145, no. 2, February 2004, pp. 799–808, DOI:10.1210/en.2003-0940
- **Nestler, J.**, et al. "Decreases in ovarian cytochrome P450c17 alpha activity and serum free testosterone after reduction of insulin secretion in polycystic ovarian syndrome", *New England Journal of Medicine*, vol. 335, no. 9, 1996, pp. 657-65, DOI: 10.1056/NEJM199608293350902
- **Rourke, K.A.**, et al. "Mechanism of action of spironolactone on cortisol production by guinea pig adrenocortical cells," *Molecular & Cellular Endocrinology*, vol. 81, no. 1-3, October 1991, pp. 127-34, DOI: 10.1016/0303-7207(91)90211-a
- Ueshiba, H., et al., "Decreased steroidogenic enzyme 17,20-lyase and increased 17-hydroxylase activities in Type 2 Diabetes mellitus", *European Journal of Endocrinology*, vol. 146, no. 3, March 2002, pp. 375-80, DOI: 10.1530/eje.0.1460375
- **Weber, M.M.**, et al., "Different inhibitory effect of etomidate and ketoconazole on the human adrenal steroid biosynthesis", *The Clinical Investigator*, vol. 71, no. 11, November 1993, pp. 933-8, DOI: 10.1007/bf00185607

3. CYP17A (17,20 lyase)

- **Bird, I.M.** and Abbott, D.H. "The hunt for a selective 17,20 lyase inhibitor; learning lessons from nature", *Journal of Steroid Biochemistry & Molecular Biology*, vol.163, October 2016, pp. 136-46, doi: 10.1016/j.jsbmb.2016.04.021.
- **Deluca, D.** et al. "Inhibition of 17beta-hydroxysteroid dehydrogenases by phytoestrogens: Comparison with other steroid metabolizing enzymes", *The Journal of Steroid Biochemistry & Molecular Biology*, vol. 93, no. 2-5, February 2005, pp. 285-292, DOI:10.1016/j.jsbmb.2004.12.035
- **Nelson-Degrave, V.L.**, et al., "Valproate Potentiates Androgen Biosynthesis in Human Ovarian Theca Cells", *Endocrinology*, vol. 145, no. 2, February 2004, pp. 799–808, DOI:10.1210/en.2003-0940
- **Stomati, M.**, et al. "Six-month oral dehydroepiandrosterone supplementation in early and late postmenopause," *Gynecological Endocrinology*, vol. 14, no. 5, 2000, pp. 342–363, DOI:10.3109/09513590009167703
- Ueshiba, H., et al., "Decreased steroidogenic enzyme 17,20-lyase and increased 17-hydroxylase activities in Type 2 Diabetes mellitus", *European Journal of Endocrinology*, vol. 146, no. 3, March 2002, pp. 375-80, DOI: 10.1530/eje.0.1460375

STEROIDOGENESIS PATHWAYS REFERENCES

- **Weber, M.M.**, et al., "Different inhibitory effect of etomidate and ketoconazole on the human adrenal steroid biosynthesis", *The Clinical Investigator*, vol. 71, no. 11, November 1993, pp. 933-8, PMID: 8312688

4. 17 β -Hydroxysteroid Dehydrogenase (17 β -HSD)

- Armanini, D., et al. "Reduction of Serum Testosterone in Men by Licorice", *New England Journal of Medicine*, vol. 341, no.15, October 1999, pp.1158-1158, DOI: 10.1056/NEJM199910073411515
- **Deluca, D.** et al. "Inhibition of 17beta-hydroxysteroid dehydrogenases by phytoestrogens: Comparison with other steroid metabolizing enzymes", *The Journal of Steroid Biochemistry & Molecular Biology*, vol. 93, no. 2-5, February 2005, pp. 285-292, DOI:10.1016/j.jsbmb.2004.12.035
- Le Bail, J., et al., "Aromatase and 17 β -hydroxysteroid dehydrogenase inhibition by flavonoids", *Cancer Letters*, vol. 133, no. 1, November 1998, pp. 101-106, DOI: 10.1016/s0304-3835(98)00211-0
- Schuster, D., et al., "Discovery of nonsteroidal 17beta-hydroxysteroid dehydrogenase 1 inhibitors by pharmacore-based screening of virtual libraries", *Journal of Medicinal Chemistry*, vol. 51, no. 14, July 2008, 4188-4199, DOI: 10.1021/jm800054h

5. 3 β -HSD

- DeClue, T.J., et al., "Insulin Resistance and Hyperinsulinemia Induce Hyperandrogenism in a Young Type B Insulin-Resistant Female", *The Journal of Clinical Endocrinology & Metabolism*, vol. 72, no. 6, June 1991, pp. 1308-1311, DOI: 10.1210/jcem-72-6-1308
- **Deluca, D.** et al. "Inhibition of 17beta-hydroxysteroid dehydrogenases by phytoestrogens: Comparison with other steroid metabolizing enzymes", *The Journal of Steroid Biochemistry & Molecular Biology*, vol. 93, no. 2-5, February 2005, pp. 285-292, DOI:10.1016/j.jsbmb.2004.12.035
- Pang, S., "Congenital Adrenal Hyperplasia Owing to 3 β -Hydroxysteroid Dehydrogenase deficiency", *Endocrinology and Metabolism Clinics of North America*, vol. 30, no. 1, March 2001, 81-99, DOI: 10.1016/s0889-8529(08)70020-3
- **Rasmussen, M.K.**, et al., "Regulation of 3 β -Hydroxysteroid Dehydrogenase/ Δ 5- Δ 4 Isomerase: A Review", *International Journal of Molecular Sciences*, vol.14, no. 9, September 2013, pp. 17926-17942; doi:10.3390/ijms140917926
- Sato, K., et al., "Resistance training restores muscle sex steroid hormone steroidogenesis in older men", *The FASEB Journal*, vol. 28, no. 4 , April 2014, pp. 1891-1897, DOI: 10.1096/fj.13-245480
- Strauss, J.F., "Some New Thoughts on the Pathophysiology and Genetics of Polycystic Ovary Syndrome", *Annals of the New York Academy of Sciences*, vol. 997, no. 1, November 2003, pp. 42-48, DOI: 10.1196/annals.1290.005

6. 5 α -reductase

- **Azzouni, F.**, et al. "The 5 Alpha-Reductase Isozyme Family: A Review of Basic Biology and Their Role in Human Diseases", *Advances in Urology*, vol. 2012, no. 530121, 2012, doi:10.1155/2012/530121
- Baudrand, R.C.A., et al., "Overexpression of hepatic 5 α -reductase and 11 β -hydroxysteroid dehydrogenase type 1 in visceral adipose tissue is associated with hyperinsulinemia in morbidly obese patients", *Metabolism*, vol. 60, no. 12, December 2011, pp. 1775-1780, DOI: 10.1016/j.metabol.2011.05.001
- Cho, Y.H., et al. "Effect of Pumpkin Seed Oil on Hair Growth in Men with Androgenetic Alopecia: A Randomized, Double-Blind, Placebo-Controlled Trial", *Evidence Based Complementary & Alternative Medicine*, 2014, pp. 1-7, doi: 10.1155/2014/549721

STEROIDOGENESIS PATHWAYS REFERENCES

- Evans, B.A.J., et al., "Inhibition of 5-reductase in genital skin fibroblasts and prostate tissue by dietary lignans and isoflavonoids", *Journal of Endocrinology*, vol. 147, no. 2, November 1995, pp. 295-302, DOI: 10.1677/joe.0.1470295
- Ghorbanibirgani, A., et al., "The Efficacy of Stinging Nettle (*Urtica Dioica*) in Patients with Benign Prostatic Hyperplasia: A Randomized Double-Blind Study in 100 Patients", *Iranian Red Crescent Medical Journal*, vol. 15, no. 1, 2013, pp. 9-10, DOI: 10.5812/ircmj.2386
- Hong, H., et al., "Effects of pumpkin seed oil and saw palmetto oil in Korean men with symptomatic benign prostatic hyperplasia", *Nutrition Research and Practice*, vol. 3, no. 4, December 2009, 323-27, doi: 10.4162/nrp.2009.3.4.323
- Nahata, A. and Dixit, V.K., "Evaluation of 5 α -reductase inhibitory activity of certain herbs useful as antiandrogens", *Andrologia*, vol. 46, no. 6, August 2014, pp. 592-601. doi: 10.1111/and.12115. Epub 2013 May 26.
- Noguchi, M., et al. "Randomized clinical trial of an ethanol extract of *Ganoderma Lucidum* in men with lower urinary tract symptoms" *Asian Journal Andrology*, vol. 10, no. 5, September 2008, pp. 777-785, DOI: 10.1111/j.1745-7262.2008.00361.x
- Ryu, Y.W., et al., "Comparison of Tamsulosin Plus *Serenoa Repens* with Tamsulosin in the Treatment of Benign Prostatic Hyperplasia in Korean Men: 1-Year Randomized Open Label Study", *Urologia Internationalis*, vol. 94, no. 2, 2015, pp. 187-193, DOI: 10.1159/000366521
- **Stomati, M.**, et al. "Six-month oral dehydroepiandrosterone supplementation in early and late postmenopause," *Gynecological Endocrinology*, vol. 14, no. 5, 2000, pp. 342–363, DOI:10.3109/09513590009167703
- Tomlinson, J.W., et al., "Impaired Glucose Tolerance and Insulin Resistance Are Associated With Increased Adipose 11-Hydroxysteroid Dehydrogenase Type 1 Expression and Elevated Hepatic 5-Reductase Activity", *Diabetes*, vol. 57, no.10, October 2008, pp. 2652-2660, DOI: 10.2337/db08-0495
- Wu, C., et al. "5 α -reductase activity in women with polycystic ovary syndrome: a systematic review and meta-analysis", *Reproductive Biology and Endocrinology*, vol. 15, no. 21, March 2017, pp. 1-9, DOI 10.1186/s12958-017-0242-9
- **Yarnell, E.** "Botanical 5 α -Reductase Inhibitors", URL: [http://student-doctor.dryarnell.com/2019/01/11/botanical-5 \$\alpha\$ -reductase-inhibitors/](http://student-doctor.dryarnell.com/2019/01/11/botanical-5%25alpha-reductase-inhibitors/) Accessed October 22, 2019

7. 21-Hydroxylase (CYP21)

- Doleschall, M., et al. "Steroid 21-hydroxylase deficiency, the most frequent cause of congenital adrenal hyperplasia", *Orvosi Hetilap*, vol. 159, no. 7, February 2018, pp. 269-277, doi: 10.1556/650.2018.30986.
- **Malikova, J.L.**, et al., "CYP17A1 inhibitor abiraterone, an anti-prostate cancer drug, also inhibits the 21-hydroxylase activity of CYP21A2", *Journal of Steroid Biochemistry and Molecular Biology*, vol. 174, November 2017, pp. 192-200. doi: 10.1016/j.jsbmb.2017.09.007.
- Nimkarn, S., et al. "Steroid 21 Hydroxylase Deficiency Congenital Adrenal Hyperplasia", *Pediatric Clinics of North America*, vol. 58, no. 5, October 2011, pp.1281-1300, DOI: 10.1016/j.pcl.2011.07.012
- **Stomati, M.**, et al. "Six-month oral dehydroepiandrosterone supplementation in early and late postmenopause," *Gynecological Endocrinology*, vol. 14, no. 5, 2000, pp. 342–363, DOI:10.3109/09513590009167703

8. Aromatase (CYP19A1)

- **Balunas, M.J.**, et al., "Natural Products as Aromatase Inhibitors", *Anticancer Agents in Medicinal Chemistry*, vol. 8, no. 6, August 2008, pp. 646–682, PMID: 18690828
- **Balunas, M.J.** and Kinghorn, A.D. "Natural Product Compounds with Aromatase Inhibitory Activity: An Update", *Planta Medica*, vol. 76, no. 11, August 2010, pp. 1087–1093, doi:10.1055/s-0030-1250169.

STEROIDOGENESIS PATHWAYS REFERENCES

- **Bhowmik, D.,** et al. "A potential medicinal importance of zinc in human health and chronic disease", *International Journal of Pharmacy and Biomedical Sciences*, vol. 1, no. 1, 2010, pp. 5-11
- Brown, K., et al. "Metformin inhibits aromatase expression in human breast adipose stromal cells via stimulation of AMP-activated protein kinase", *Breast Cancer Research and Treatment*, vol. 123, no. 2, September 2010, pp. 591–596, DOI: 10.1007/s10549-010-0834-y
- **Chen, S.,** et al., "Anti-Aromatase Activity of Phytochemicals in White Button Mushrooms (*Agaricus bisporus*)", *Cancer Research*, vol. 66, no 24, December 2006, pp. 12026-34, doi:10.1158/0008-5472.CAN-06-2206
- Czech, U. et al., "Effect of free fatty acids on CYP19A1 (aromatase) gene expression in human adipose tissue stromal vascular fraction cells", *Przegląd Lekarski*, vol. 73, no. 5, January 2016, pp. 296-300, PMID: 29629743
- **Deluca, D.,** et al. "Inhibition of 17beta-hydroxysteroid dehydrogenases by phytoestrogens: Comparison with other steroid metabolizing enzymes", *The Journal of Steroid Biochemistry & Molecular Biology*, vol. 93, no. 2-5, February 2005, pp. 285-292, DOI:10.1016/j.jsbmb.2004.12.035
- Edmunds, K., et al. "The effects of dietary phytoestrogens on aromatase activity in human endometrial stromal cells", *Reproduction Nutrition Development*, vol. 45, no. 6, 2005, pp. 709-720, DOI: 10.1051/rnd:2005055
- Eng, E., et al. "Suppression of aromatase (estrogen synthetase) by red wine phytochemicals", *Breast Cancer Research and Treatment*, vol. 67, no. 2, May 2001, pp. 133-146, DOI:10.1023/a:1010641102147
- **Gonzalez, A.,** et al. "Melatonin: A Molecule for Reducing Breast Cancer Risk", *Molecules*, vol. 23, E336, 2018, pp. 1-21, doi: 10.3390/molecules23020336
- Grube, B., et al., "White Button Mushroom Phytochemicals Inhibit Aromatase Activity and Breast Cancer Cell Proliferation", *The Journal of Nutrition*, vol. 131, no. 12, December 2001, pp. 3288-3293, DOI:10.1093/jn/131.12.3288
- Harris, R., et al., "Cyclooxygenase-2 and the inflammation of breast cancer", *World Journal of Clinical Oncology*, vol. 5, no. 4, October 2014, pp. 677-92, doi: 10.5306/wjco.v5.i4.677
- **Higley, E.B.,** et al., "Assessment of chemical effects on aromatase activity using the H295R cell line", *Environmental Science and Pollution Research International*, vol. 17, no. 5, June 2010, pp. 1137-48, DOI 10.1007/s11356-009-0285-3
- Howe, L., et al. "Molecular Pathways: Adipose Inflammation as a Mediator of Obesity-Associated Cancer", *Clinical Cancer Research*, vol. 19, no. 22, November 2013, pp. 6074-6083, DOI: 10.1158/1078-0432.CCR-12-2603
- Kitawaki, J., et al. "Leptin directly stimulates aromatase activity in human luteinized granulosa cells", *Molecular Human Reproduction*, vol. 5, no. 8, August 1999, pp. 708–713, DOI: 10.1093/molehr/5.8.708
- Magoffin, D.A., "Leptin regulation of aromatase activity in adipose stromal cells from regularly cycling women," *Ginekologia Polska*, vol. 79, no. 1, January 1999, 1-7, PMID:10349800
- Morris, P., et al. "Inflammation and Increased Aromatase Expression Occur in the Breast Tissue of Obese Women with Breast Cancer," *Cancer Prevention Research*, vol. 4, no. 7, July 2011, pp. 1021-1029, doi: 10.1158/1940-6207.CAPR-11-0110.
- Nooshin, E., et al. "Melatonin, an inhibitory agent in breast cancer", *Breast Cancer*, vol. 24, no. 1, January 2017, pp. 42-51, doi: 10.1007/s12282-016-0690-7
- Park, Y.J., et al. "Inhibitory Aromatase Effects of Flavonoids from Ginkgo Biloba Extracts on Estrogen Biosynthesis", *Asian Pacific Journal of Cancer Prevention*, vol. 16, 2015, pp. 6317-6325, DOI: 10.7314/apjcp.2015.16.15.6317
- Rice, R., et al. "Metformin Inhibits Aromatase via an Extracellular Signal-Regulated Kinase-Mediated Pathway", *Endocrinology*, vol. 150, no. 10, October 2009, pp. 4794-4801, DOI:10.1210/en.2009-0540
- **Sanderson, J.T.,** et al. "Induction and Inhibition of Aromatase (CYP19) Activity by Various
- Classes of Pesticides in H295R Human Adrenocortical Carcinoma Cells", *Toxicology and Applied Pharmacology*, vol. 182, no. 1, July 2002, pp. 44–54, doi:10.1006/taap.2002.9420

STEROIDOGENESIS PATHWAYS REFERENCES

- Šmuc, T., et al., "Expression analysis of the genes involved in estradiol and progesterone action in human ovarian endometriosis," *Gynecological Endocrinology*, vol. 23, no. 2, 2007, pp. 105-111, DOI: 10.1080/09513590601152219
- Wang, W., et al. "Involvement of CRH and hCG in the induction of aromatase by cortisol in human placental syncytiotrophoblasts", *Placenta*, vol. 35, no. 1, January 2014, pp. 30–36, doi:10.1016/j.placenta.2013.10.018.
- Wang, X., et al. "Aromatase overexpression in dysfunctional adipose tissue links obesity to postmenopausal breast cancer", *The Journal of Steroid Biochemistry and Molecular Biology*, vol. 153, September 2015, pp. 35-44, doi: 10.1016/j.jsbmb.2015.07.008
- Zhang, Y., et al. "Extraction, isolation, and aromatase inhibitory evaluation of low-polar ginsenosides from *Panax ginseng* leaves," *Journal of Chromatography A*. vol. 1483, February 2017, pp. 20-29, doi: 10.1016/j.chroma.2016.12.068.

9. CYP1A1

- Dalessandri, K., et al., "Pilot Study: Effect of 3,3' -Diindolylmethane Supplements on Urinary Hormone Metabolites in Postmenopausal Women With a History of Early-Stage Breast Cancer", *Nutrition and Cancer*, vol. 50, no. 2, 2004, pp.161-167, DOI: 10.1207/s15327914nc5002_5
- **He, S.** et al. "Iodine stimulates estrogen receptor singling and its systemic level is increased in surgical patients due to topical absorption", *Oncotarget*, vol. 9, no. 1, 2018, pp. 375-384, <https://doi.org/10.18632/oncotarget.20633>
- Hodges, R., et al. "Modulation of metabolic detoxification pathways using foods and food-derived components: a scientific review with clinical application", *Journal of Nutrition & Metabolism*, 2015;2015:760689, doi: 10.1155/2015/760689
- **Li, Fei** et al. "Potential role of CYP1B1 in the development and treatment of metabolic diseases", *Pharmacology & Therapeutics*, vol. 178, October 2017, pp.18–30, doi:10.1016/j.pharmthera.2017.03.007.
- Lu, L., et al., "Increased urinary excretion of 2-hydroxyestrone but not 16alpha-hydroxyestrone in premenopausal women during a soya diet containing isoflavones", *Cancer Research*, vol. 60, no. 5, March 2000, pp. 1299-1305, PMID: 10728690
- **Michnovicz, J.**, et al. "Increased estrogen 2-hydroxylation in obese women using oral indole-3-carbinol", *International Journal of Obesity*, vol. 22, no. 3, 1998, pp. 227-229, DOI:10.1038/sj.ijo.0800573
- **Mistacka, R.** et al. "Inhibition of human recombinant cytochromes P450 CYP1A1 and CYP1B1 by trans-resveratrol methyl ethers", *Molecular Nutrition & Food Research*, vol. 51, no. 5, May 2007, pp. 517 – 524, DOI 10.1002/mnfr.200600135
- Peters, L., et al., "Effect of high sucrose diet on cytochrome P450 1A and heterocyclic amine mutagenesis", *Anticancer Research*, vol. 23, no. 1A, 2003, pp. 399-403, PMID: 12680239
- **Poor, A.E.**, et al., et al. "Urine Iodine, Estrogen, and Breast Disease", *Journal of Cancer Therapy*, vol. 3, no. 6, December 2012, pp. 1164-1169, <http://dx.doi.org/10.4236/jct.2012.36152>
- **Santes-Palacios, R** et al. Inhibition of human and rat CYP1A1 enzyme by grapefruit juice compounds. *Toxicology Letters*, vol. 258, September 2016, pp. 267-275. doi: 10.1016/j.toxlet.2016.07.023. Epub 2016 Jul 18.
- Stoddard, F., et al., "Iodine Alters Gene Expression in the MCF7 Breast Cancer Cell Line: Evidence for an Anti-Estrogen Effect of Iodine", *International Journal of Medical Sciences*, vol. 5, no. 4, July 2008, pp. 189-196, DOI:10.7150/ijms.5.189
- Terry, P., et al., "Brassica vegetables and breast cancer risk", *JAMA*, vol. 285, no. 23, June 2001, pp. 2975-2977, DOI: 10.1001/jama.285.23.2975

STEROIDOGENESIS PATHWAYS REFERENCES

10. CYP1B1

- Chang, T., et al. "Effect of Ginkgo biloba extract on procarcinogen-bioactivating human CYP1 enzymes: Identification of isohamnetin, kaempferol, and quercetin as potent inhibitors of CYP1B1", *Toxicology and Applied Pharmacology*, vol. 213, no. 1, May 2006, pp. 18-26, DOI: 10.1016/j.taap.2005.09.007
- **Dutour, R.** and Poirier, D. "Inhibitors of Cytochrome (CYP) P450 B1", *European Journal of Medicinal Chemistry*, vol. 135, July 2007, pp. 296-306, DOI:10.1016/j.ejmech.2017.04.042
- Ghisari, M., et al. "Genetic polymorphisms in CYP1A1, CYP1B1 and COMT genes in Greenlandic Inuit and Europeans", *International Journal of Circumpolar Health*, vol. 72, no. 1, June 2013, 21113, pp. 1-9, doi: 10.3402/ijch.v72i0.21113.
- Girennavar, B., et al. "Furocoumarins from grapefruit juice and their effect on human CYP 3A4 and CYP 1B1 isoenzymes," *Bioorganic & Medicinal Chemistry*, vol.14, no.8, December 2005, pp. 2606-12, DOI:10.1016/j.bmc.2005.11.039
- **He, S.** et al. "Iodine stimulates estrogen receptor signaling and its systemic level is increased in surgical patients due to topical absorption", *Oncotarget*, vol. 9, no. 1, 2018, pp. 375-384, <https://doi.org/10.18632/oncotarget.20633>
- Korobkova, E., "Effect of Natural Polyphenols on CYP Metabolism: Implications for Diseases", *Chemical Research in Toxicology*, vol. 28, no. 7, 2015, pp. 1359-1390, doi: 10.1021/acs.chemrestox.5b00121
- **Li, Fei** et al. "Potential role of CYP1B1 in the development and treatment of metabolic diseases", *Pharmacology & Therapeutics*, vol. 178, October 2017, pp.18-30, doi:10.1016/j.pharmthera.2017.03.007.
- **Madhubhani, L.P.** et al., "Hops (*Humulus lupulus*) inhibits Oxidative Estrogen Metabolism and Estrogen-Induced Malignant Transformation in Human Mammary Epithelial cells (MCF-10A)", *Cancer Prevention Research*, vol. 5, no. 1, January 2012, pp. 73-81, doi:10.1158/1940-6207.CAPR-11-0348.
- Mammen, J., et al. "Coumarins are competitive inhibitors of cytochrome P450 1B1, with equal potency for allelic variants", *Pharmacogenetics & Genomics*, vol. 15, no. 3, March 2005, pp.183-188, PMID: 15861043
- **Shimada, T.** and Fujii-Kuriyama, Y. "Metabolic activation of polycyclic aromatic hydrocarbons to carcinogens by cytochromes P450 1A1 and 1B1", *Cancer Science*, vol. 95, no. 1, January 2004, pp. 1-6, DOI: 10.1111/j.1349-7006.2004.tb03162.x

11. CYP3A4

- **Basheer, L.** and Karem, Z., "Interactions between CYP3A4 and Dietary Polyphenols", *Oxidative Medicine and Cellular Longevity*, Volume 2015, 854015, pp. 1-15, <http://dx.doi.org/10.1155/2015/854015>
- Fukuda, K., et al., "Specific CYP3A4 Inhibitors in Grapefruit Juice: Furocoumarin Dimers as Components of Drug Interaction", *Pharmacogenetics*, vol. 7, no. 5, October 1997, pp. 391-396, DOI:10.1097/00008571-199710000-00008
- Goey, A., et al. "The Effect of St John's Wort on the Pharmacokinetics of Docetaxel", *Clinical Pharmacokinetics*, vol. 53, no. 1, January 2014, pp. 103-110, DOI: 10.1007/s40262-013-0102-5
- **Gurley, B.**, et al., "In Vivo Effects of Goldenseal, Kava Kava, Black Cohosh, and Valerian on Human Cytochrome P450 1A2, 2D6, 2E1, and 3A4/5 Phenotypes", *Clinical Pharmacology & Therapeutics*, vol. 77, no. 5, May 2005, pp. 415-426, DOI: 10.1016/j.clpt.2005.01.009
- **Hanley, M.J.**, et al., "The effect of grapefruit juice on drug disposition", *Expert Opinion on Drug Metabolism & Toxicology*, vol. 7, no. 3, March 2011, pp. 267-286, doi:10.1517/17425255.2011.553189.
- **Horn, J.R.** and Hansten, P.D. "Get to Know an Enzyme: CYP 3A4", *Pharmacy Times*, September 2008
- **Iwata, H.** et al., "Identification and characterization of potent CYP3A4 inhibitors in Schisandra fruit extract", *Drug Metabolism & Disposition*, vol. 32, no. 12, December 2004, pp.1351-8, DOI: 10.1124/dmd.104.000646

STEROIDOGENESIS PATHWAYS REFERENCES

- Komoroski, B., et al. "Induction And Inhibition Of Cytochromes P450 By The St. Johns Wort Constituent Hyperforin In Human Hepatocyte Cultures", *Drug Metabolism and Disposition*, vol. 32, no. 5, May 2004, pp. 512-18, DOI: 10.1124/dmd.32.5.512
- **Nowak, R.** "Review Article: Cytochrome P450 enzyme, and transport protein mediated herb–drug interactions in renal transplant patients: Grapefruit juice, St John's Wort – and beyond", *Nephrology*, vol. 13, no. 4, June 2008, pp. 337–347, doi:10.1111/j.1440-1797.2008.00940.x

12. COMT (Catechol-O-Methyltransferase)

- Anderson, O., et al., "Nutrition and epigenetics: an interplay of dietary methyl donors, one-carbon metabolism, and DNA methylation," *Journal of Nutritional Biochemistry*, vol. 23, August 2012, pp. 853-859, doi: 10.1016/j.jnutbio.2012.03.003.
- **Bonafacio, M.J.** et al., "Catechol-O-methyltransferase and Its Inhibitors in Parkinson's Disease", *CNS Drug Reviews*, vol. 13, no. 3, 2007, pp. 352-79, <https://doi.org/10.1111/j.1527-3458.2007.00020.x>
- **Goodman, J.E.**, et al. "COMT genotype, micronutrients in the folate metabolic pathway and breast cancer risk", *Carcinogenesis*, vol. 22, no. 10, October 2001, 1661-65, DOI: 10.1093/carcin/22.10.1661
- Hodges, R., et al. "Modulation of metabolic detoxification pathways using foods and food-derived components: a scientific review with clinical application", *Journal of Nutrition & Metabolism*, 2015:760689, October 2015, doi: 10.1155/2015/760689
- **Wang, Piwen** et al., "Quercetin increased bioavailability and decreased methylation of green tea polyphenols in vitro and in vivo", *Food & Function*, vol. 3, no. 6, June 2012, pp. 635–642, doi:10.1039/c2fo10254d
- Waters, C. "Catechol-O-Methyltransferase (COMT) inhibitors in Parkinson's disease", *Journal of American Geriatric Society*, vol. 48, no. 6, June 2000, pp.692-698, doi.org/10.1111/j.1532-5415.2000.tb04732.x
- Woods, J., et al., "Genetic Polymorphisms of Catechol-O-Methyltransferase Modify the Neurobehavioral Effects of Mercury in Children", *Journal of Toxicology and Environmental Health*, vol. 77, no. 6, January 2014, pp. 293-312, DOI: 10.1080/15287394.2014.867210
- Zhu, B.T. et al., "Inhibition of Human Catechol-O-Methyltransferase (COMT)-Mediated O-Methylation of Catechol Estrogens by Major Polyphenolic Components Present in Coffee *Journal of Steroid Biochemistry & Molecular Biology*, vol. 113, no. 1-2, January 2009, pp. 65–74, DOI: 10.1016/j.jsbmb.2008.11.011

13. CYP11B1

- Hille, U.E., et al., "First Selective CYP11B1 Inhibitors for the Treatment of Cortisol-Dependent Diseases", *ACS Medicinal Chemistry Letters*, vol. 2, no. 1, October 2010, pp. 2–6, DOI:10.1021/ml100071j
- **Puglisi, S.** et al., "Preoperative treatment with metyrapone in patients with Cushing's syndrome due to adrenal adenoma: a pilot prospective study", *Cancer Research*, vol. 7, no. 11, November 2018, 1227-35, <https://doi.org/10.1530/EC-18-0400>
- **Stomati, M.**, et al. "Six-month oral dehydroepiandrosterone supplementation in early and late postmenopause," *Gynecological Endocrinology*, vol. 14, no. 5, 2000, pp. 342–363, DOI:10.3109/09513590009167703

14. CYP11B2

- Freel, E.M., et al., "Effect of variation in CYP11B1 and CYP11B2 on corticosteroid phenotype and hypothalamic-pituitary-adrenal axis activity in hypertensive and normotensive subjects", *Clinical Endocrinology*, vol. 68, no. 5, April 2008, pp. 700-6, DOI: 10.1111/j.1365-2265.2007.03116.x

STEROIDOGENESIS PATHWAYS REFERENCES

- **Hoyt, S.B.**, et al., "Discovery of indazole aldosterone synthase (CYP11B2) inhibitors as potential treatments for hypertension", *Bioorganic & Medicinal Chemistry Letters*, vol. 27, no. 11, June 2017, pp. 2384-88, DOI: 10.1016/j.bmcl.2017.04.021

15. 11 β -HSD Type 1 & 2

- Atanasov, A.G., et al., "Coffee inhibits the reactivation of glucocorticoids by 11beta-hydroxysteroid dehydrogenase type 1: a glucocorticoid connection in the anti-diabetic action of coffee?" *FEBS Letters*, vol. 580, no. 17, July 2006, pp. 4081-5, DOI: 10.1016/j.febslet.2006.06.046
- Cai, T.Q., et al., "Induction of 11beta-hydroxysteroid dehydrogenase type 1 but not -2 in human aortic smooth muscle cells by inflammatory stimuli", *Journal of Steroid Biochemistry & Molecular Biology*, vol. 77, no. 2-3, May 2001, pp. 117-22, [https://doi.org/10.1016/S0960-0760\(01\)00041-3](https://doi.org/10.1016/S0960-0760(01)00041-3)
- **Chapman, K.**, et al., 11 β -Hydroxysteroid Dehydrogenases: Intracellular Gate-Keepers of Tissue Glucocorticoid Action, *Physiologic Reviews*, vol. 93, no. 3, July 2013, 1139–1206, doi: 10.1152/physrev.00020.2012
- Chapman, K., et al., "Changing glucocorticoid action: 11 β -hydroxysteroid dehydrogenase type 1 in acute and chronic inflammation", *Journal of Steroid Biochemistry & Molecular Biology*, vol. 137, September 2013, pp. 82-92. doi: 10.1016/j.jsbmb.2013.02.002.Epub 2013 Feb 19.
- **Diederich, S.**, et al., "In the search for specific inhibitors of human 11b-hydroxysteroid-dehydrogenases (11b-HSDs): chenodeoxycholic acid selectively inhibits 11b-HSD-I", *European Journal of Endocrinology*, vol. 142, no. 2, February 2000, pp. 200–207, DOI:10.1530/eje.0.1420200
- Ferrari, P., et al., "In vivo 11beta-HSD-2 activity: variability, salt-sensitivity, and effect of licorice", *Hypertension*, vol. 38, no. 6, December 2000, 1330-6, DOI: 10.1161/hy1101.096112
- Hoshiro, M., et al., "Comprehensive study of urinary cortisol metabolites in hyperthyroid and hypothyroid patients", *Clinical Endocrinology (Oxford)*, vol. 64, no. 1, January 2006, pp. 37-45, DOI: 10.1111/j.1365-2265.2005.02412.x
- **Hu, G-X.**, et al., "Curcumin as a Potent and Selective Inhibitor of 11b-Hydroxysteroid Dehydrogenase 1: Improving Lipid Profiles in High-Fat-Diet-Treated Rats", *PLoS ONE*, vol. 8, no. 3, March 2013, e49976, doi:10.1371/journal.pone.0049976
- Seckl, J.R., et al., "Glucocorticoids and 11beta-Hydroxysteroid Dehydrogenase in Adipose Tissue", *Recent Prog Horm Res.* vol. 59, Chapter 17, 2004, pp. 359-93, PMID:14749510
- Stiefel P., et al., "Role of ketoconazole treatment in urinary-free cortisol-to-cortisone and tetrahydrocortisol-to-tetrahydrocortisone ratios in nonectopic Cushing's syndrome", *Endocrine*, vol. 18, no. 3, August 2002, pp. 279-84, DOI: 10.1385/ENDO:18:3:279
- Taniyama, M., et al. "Urinary cortisol metabolites in the assessment of peripheral thyroid hormone action: application for diagnosis of resistance to thyroid hormone", *Thyroid*, vol. 3, no. 3, 1993, pp. 229-33, DOI: 10.1089/thy.1993.3.229
- Van Umm, S.H., "Licorice and Hypertension", *Netherlands Journal of Medicine*, vol. 63, no. 4, April 2005, pp.119-20, PMID: 15869038
- **Walker, B.**, and Seckl, J. "Cortisol Metabolism" *International Textbook of Obesity*, Edited by Per Bjorntorp, John Wiley & Sons Ltd. 2001. 241-268.

16. Sulfotransferase & Sulfatase

- **Coughtrie, M.W.H.** and Johnston, L.E., "Interactions Between Dietary Chemicals and Human Sulfotransferases — Molecular Mechanisms and Clinical Significance", *Drug Metabolism and Disposition*, vol. 29, no. 4, Part 2, 2001, pp. 522-28, PMID: 11259344.

STEROIDOGENESIS PATHWAYS REFERENCES

- **Feng, Y.**, et al., "Hepatic steroid sulfatase critically determines estrogenic activities of conjugated equine estrogens in human cells in vitro and in mice", *Journal of Biological Chemistry*, vol. 294, August 2019, pp. 12112-21, doi: 10.1074/jbc.RA119.009181
- **Gonzalez, A.**, et al., "Melatonin affects the dynamic steady-state equilibrium of estrogen sulfates in human umbilical vein endothelial cells by regulating the balance between estrogen sulfatase and sulfotransferase," *International Journal of Molecular Medicine*, vol. 36, no. 6, December 2015, pp. 1671-6. DOI:10.3892/ijmm.2015.2360
- Jiang, M., et al., "Inflammatory regulation of steroid sulfatase: A novel mechanism to control estrogen homeostasis and inflammation in chronic liver disease", *Journal of Hepatology*, vol. 64, no. 1, January 2016, pp. 44-52, doi: 10.1016/j.jhep.2015.07.022. Epub 2015 Jul 26
- **Kester, M.H.A.** et al. "Sulfation of Thyroid Hormone by Estrogen Sulfotransferase", *The Journal of Clinical Endocrinology & Metabolism*, vol. 84, no.7, July 1999, pp. 2577-80, DOI: 10.1210/jcem.84.7.5975.
- **King, R.S.**, et al., "Inhibition of human phenol and estrogen sulfotransferase by certain non-steroidal anti-inflammatory agents", *Current Drug Metabolism*, vol. 7, no. 7, October 2006, pp. 745–753, DOI: 10.2174/138920006778520615
- **Palmieri, C.**, "Irosustat: a first-generation steroid sulfatase inhibitor in breast cancer," vol. 11, no. 2, February 2011, pp. 179-83, doi: 10.1586/era.10.201.
- **Rižner, T.L.** "The Important Roles of Steroid Sulfatase and Sulfotransferases in Gynecological Diseases", *Frontiers in Pharmacology*, vol. 7, no. 30, February 2016, pp. 1-16, doi: 10.3389/fphar.2016.00030
- **Stomati, M.**, et al. "Six-month oral dehydroepiandrosterone supplementation in early and late postmenopause," *Gynecological Endocrinology*, vol. 14, no. 5, 2000, pp. 342–363, DOI:10.3109/09513590009167703
- **Sueyoshi, T.**, et al. "Garlic Extract Diallyl Sulfide (DAS) Activates Nuclear Receptor CAR to Induce the Sult1e1 Gene in Mouse Liver-2011", *PLoS ONE*, vol. 6, no. 6, June 2011, e21229, doi:10.1371/journal.pone.0021229

Estrogens

- **Aune, D.**, et al. "Dietary fiber and breast cancer risk: a systematic review and meta-analysis of prospective studies", *Annals of Oncology*, vol. 23, no. 6, 2012, pp. 1394-1402, doi: 10.1093/annonc/mdr589. Epub 2012 Jan 10
- **Chadwick, L.R.**, et al. "The pharmacognosy of *Humulus lupulus* L. (hops) with an emphasis on estrogenic properties", *Phytomedicine*, vol. 13, no. 1-2, January 2006, pp. 119–131, doi: 10.1016/j.phymed.2004.07.006
- **Dietz, B.M.** et al., "Botanicals and Their Bioactive Phytochemicals for Women's Health", *Pharmacology Review*, vol. 68, no. 4, October 2016, pp.1026–1073, doi: 10.1124/pr.115.010843
- Dong, J., et al. "Dietary fiber intake and risk of breast cancer: a meta-analysis of prospective cohort studies", *American Journal of Clinical Nutrition*, vol. 94, no. 3, 2011, pp. 900-905, doi: 10.3945/ajcn.111.015578. Epub 2011 Jul 20.
- Porpora M., et al. A Promise in the Treatment of Endometriosis: An Observational Cohort Study on Ovarian Endometrioma Reduction by N-Acetylcysteine. *Evidence-Based Complementary and Alternative Medicine*. 2013:1-7.
- **Zahid, M.**, et al. "N-acetylcysteine blocks formation of cancer-initiating estrogen–DNA adducts in cells", *Free Radical Biology and Medicine*, vol. 49, no. 3, August 2010, pp. 392–400, doi: 10.1016/j.freeradbiomed.2010.04.028. Epub 2010 May 31.

Progesterone

- **Carlson, M.**, et al., "Catch it before it kills: Progesterone, Obesity, and the Prevention of Endometrial Cancer", *Discovery Medicine*, vol. 14, no. 76, September 2012, pp. 215-222, PMID:23021376

STEROIDOGENESIS PATHWAYS REFERENCES

- Hirofumi, H., et al. Effects of Ascorbic Acid Supplementation on Serum Progesterone Levels in Patients with a Luteal Phase Defect. *Fertility and Sterility*. 2003. 80(2):459-61.
- **Sapbamer, R.,** et al., "Effects of dietary traditional fermented soybean on reproductive hormones, lipids, and glucose among postmenopausal women in northern Thailand", *Asia Pacific Journal of Clinical Nutrition*, vol. 22, no. 2, 2013, pp. 222-228, doi: 10.6133/apjcn.2013.22.2.17.
- **Takasaki, A.,** et al. "Luteal Blood Flow and Luteal Function", *Journal of Ovarian Research*, vol. 2, no. 1, January 2009, pp. 1-6, doi: 10.1186/1757-2215-2-1
- **van Die, M.,** et al., "Vitex agnus-castus Extracts for Female Reproductive Disorders: A Systematic Review of Clinical Trials", *Planta Medica*, vol. 79, no. 7, May 2013, pp. 562–575, doi: 10.1055/s-0032-1327831. Epub 2012 Nov 7.

Cortisol

- **Bao, Ai-Min** and Swaab, Dick F., "The human hypothalamus in mood disorders: The HPA axis in the center", *IBRO Reports*, vol. 6, June 2019, pp. 45-53, doi.org/10.1016/j.ibror.2018.11.008
- **Head, K., and Kelly, G.** "Nutrients and botanicals for treatment of stress: adrenal fatigue, neurotransmitter imbalance, anxiety, and restless sleep", *Alternative Medicine Review*, vol. 14, no. 12, June 2009, pp. 114-140, PMID:19594222
- **Kimura, K.,** et al., "L-Theanine reduces psychological and physiological stress responses", *Biological Psychology*, vol. 74, no. 1, January 2007, pp. 39–45, DOI: 10.1016/j.biopsycho.2006.06.006
- Kurina, L.M., et al., "Stress, symptoms of depression and anxiety, and cortisol patterns in working parents", *Stress and Health*, vol. 20, no. 2, 2004, pp. 53-63, DOI: 10.1002/smi.998
- Römer, B., et al. "Cortisol metabolism in depressed patients and healthy controls", *Neuroendocrinology*, vol. 90, no. 3, 2009, pp. 301-306, doi: 10.1159/000235904. Epub 2009 Aug 28.
- **Starks, M.,** et al. "The effects of phosphatidylserine on endocrine response to moderate intensity exercise", *Journal of International Society of Sports Nutrition*, vol. 5, no. 11, July 2008, pp.1-6, doi: 10.1186/1550-2783-5-11.
- **Stauffer, A.T.,** et al., "Chenodeoxycholic Acid and Deoxycholic Acid Inhibit 11-Hydroxysteroid Dehydrogenase Type 2 and Cause Cortisol-induced Transcriptional Activation of the Mineralocorticoid Receptor", *Journal of Biological Chemistry*, Vol. 277, No. 29, July 2002, pp. 26286–26292, doi: 10.1074/jbc.M201556200

Testosterone

- **Kumari-Neena, D.,** et al. "Dietary zinc deficiency in man. Effect on testicular function.", *Journal of Laboratory & Clinical Medicine*, vol. 96, no. 3, 1980, pp. 544-550, PMID:6772723
- **Maheshwari, A.,** et al. "Efficacy of Furosap™, a novel *Trigonella foenum-graecum* seed extract, in Enhancing Testosterone Level and Improving Sperm Profile in Male Volunteers", *International Journal of Medical Sciences*, vol. 14, no.1, January 2017, pp. 58–66, doi: 10.7150/ijms.17256. eCollection 2017.
- **Manna, P.** et al., "Cadmium induced testicular pathophysiology: Prophylactic role of taurine", *Reproductive Toxicology*, vol. 26, no. 3-4, November-December 2008, pp. 282-291, DOI: 10.1016/j.reprotox.2008.09.009
- Midzak, A.S. et al., "Leydig cell aging and the mechanisms of reduced testosterone synthesis", *Molecular and Cellular Endocrinology*, vol. 299, no.1, February 2009, pp. 23-31, doi: 10.1016/j.mce.2008.07.016. Epub 2008 Aug 5.
- **Mohammad, N.S.,** et. al., "Coenzyme Q10 and fish oil synergistically alleviate aluminum chloride-induced suppression of testicular steroidogenesis and antioxidant defense", *Free Radical Research*, vol. 49, no. 11, 2015, pp.1319-1334, DOI:10.3109/10715762.2015.1069290

STEROIDOGENESIS PATHWAYS REFERENCES

- **Roayah, M.**, et al. "Pilot Study on the Effect of Botanical Medicine (*Tribulus terrestris*) on Serum Testosterone Level and Erectile Function in Aging Males With Partial Androgen Deficiency (PADAM)", *Journal of Sex & Marital Therapy*. Vol. 42, no. 4, May 2015, pp. 297–301, doi: 10.1080/0092623X.2015.1033579. Epub 2015 Apr 7.
- **Tambi, M.**, et al., "Standardised water-soluble extract of *Eurycoma longifolia*, Tongkat ali, as testosterone booster for managing men with late-onset hypogonadism?", *Andrologia*, vol. 44, May 2012, pp. 226–230, doi: 10.1111/j.1439-0272.2011.01168.x. Epub 2011 Jun 15.
- **Thu, H.E.** et al., "Eurycoma Longifolia as a potential adoptogen of male sexual health: a systematic review on clinical studies", *Chinese Journal of Natural Medicines*, vol. 15, no. 1, January 2017, pp. 71–80, doi: 10.1016/S1875-5364(17)30010-9.