Faculty of Science and Technology
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Exploring the potential application of glucuronides as a prognostic biomarker for disease

Volume 2: References and Appendices

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Contents

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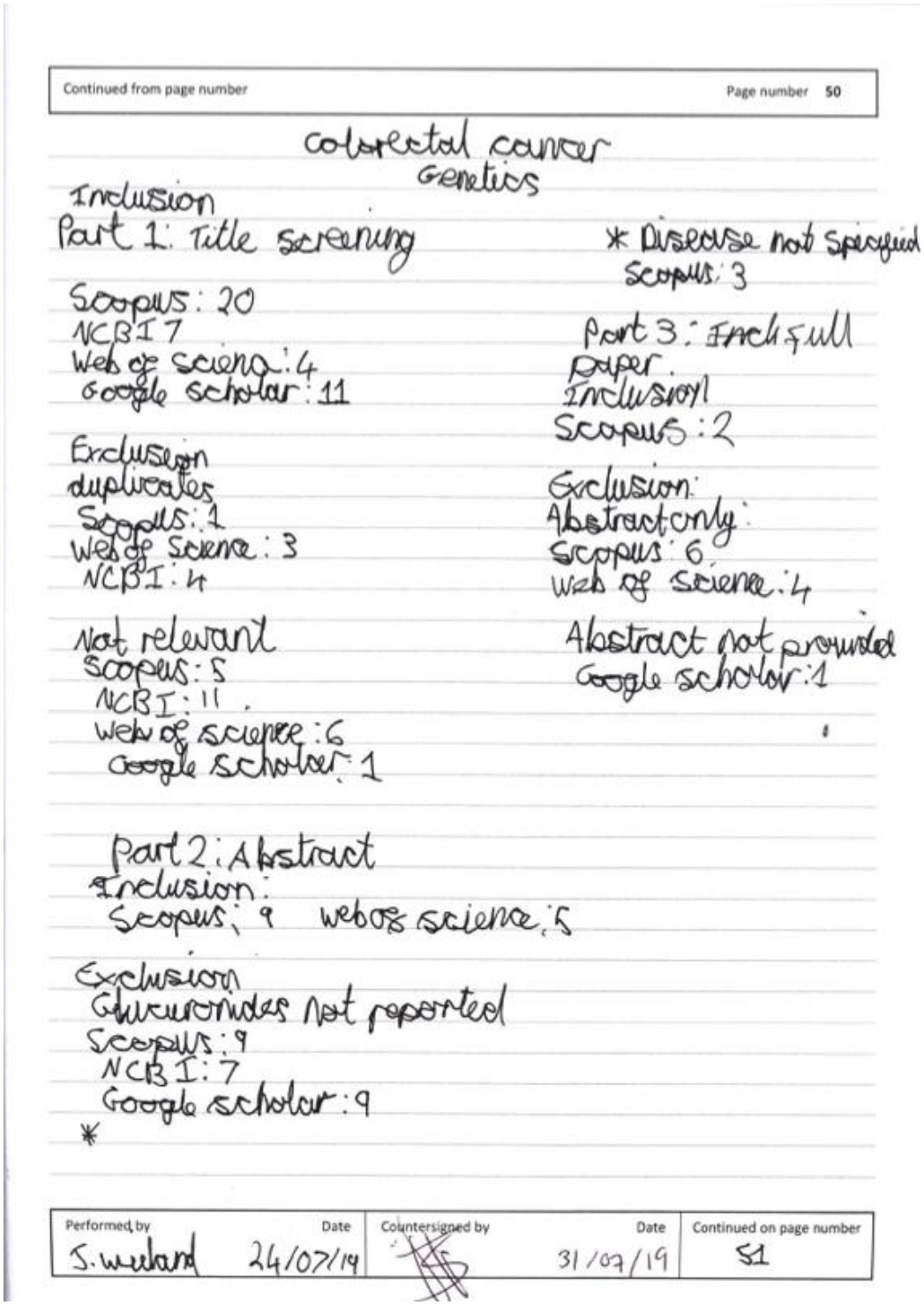
Appendices

Appendix1: Log Book Evidence for Chapter 7



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colorectal cancer
Genetics

Inclusion
Part 1: Title screening

Scopus: 20
NCBI 7
Web of scienc: 4
Google scholar: 11

Exclusion
duplicates
Scopus: 1
Web of Scienc: 3
NCBI: 4

Not relevant
Scopus: 5
NCBI: 11
Web of scienee: 6
Google scholar: 1

* Disease not specified
Scopus: 3

Part 3: Inch full paper.
Inclusion
Scopus: 2

Exclusion:
Abstract only:
Scopus: 6
Web of Scienc: 4

Abstract not provided
Google scholar: 1

Part 2: Abstract
Inclusion:
Scopus; 9 webos scienc; 5

Exclusion
Glucuronides not reported
Scopus: 9
NCBI: 7
Google scholar: 9
*

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S. weiland	24/07/19		31/07/19	51

Lyestyle

Part 1: Title Screening
Inclusion
Scopus: 7
Google Scholar: 5
NCBI: 1

Excluded
Not Relevant:
Scopus: 5

Part 2: Abstract screening
Inclusion
Scopus: 3

Exclusion:
~~ga~~ Glucuronides unreported:
Google Scholar: 2

Part 3:
Full paper analyses

Inclusion:
Scopus 1

Google scholar: 1

Exclusion
Disease unspecified
Scopus: 1

Performed by	Date	Countersigned by	Date	Continued on page number
J. Wiechard	24/07/19		31/07/19	

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Type 2 diabetes
Gebeliovs

Inclusion
part 1: title inclusion
scopus: 4
Google Scholar: 1

Exclusion
Duplicates by title:
Web of Science: 3

Not relevant:
Scopus: 5
Web of Science: 1
NCBI: 1

Part 2: Abstract
Included
Scopus: 1

Excluded
Glucuronides unreported:
Scopus: 3
Google Scholar: 1

Part 3: Full paper analysis
~~Scopus~~: Excluded: 1
Glucuronides reported that are not associated to a disease
Scopus: 1
~~Google Scholar: 2~~

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Part 1 inclusion (title) Lifestyle

Scopus: 1
Google scholar: 2

Exclusion
Duplicates by title
Scopus: 1
Web of Science 1
NCBI: 1

Not relevant:
Web of scienc: 1

Part 2: Abstract
Inclusion
Google scholar: 1
Scopus: 4

Part 3: Full paper analysis
Inclusion
Scopus 1
Google scholar: 1

Excluded
Glucuronides reported that do not comefrom human:

Scopus: 1
Google scholar: 1

Reviews (literature/systematic)
Scopus: 1

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S. Weeland	24/07/19	24/07/19	31/07/19	

Parkinson's disease
Genetics
to Inclusion: Title part 1

Scopus: 1

Exclusion

Duplicates by title:
Scopus, Web of Science 1

not relevant:
Scopus: 1
Web of Science: 4
NCBI: 1

Lifestyle
Part 1: Title screening

Exclusion
Duplicates:
Web of Science: 4
not relevant: 3

Performed by	Date	Countersigned by	Date	Continued on page number
J. Wiebard	24/07/19		31/07/19	

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Prostate Cancer
Genetics

Part 1: Inclusion (title)

NCBI: 9
Google Scholar: 10

Exclusion:
not relevant
Scopus: 1
NCBI: 9

Duplicates
Web of Science: 1
NCBI: 5
Google Scholar: 7

Part 2: Abstract

Inclusion:
NCBI: 6
Google Scholar: 2

Exclusion
Glycomimetics unreported
NCBI: 6
Google Scholar: 5

part 3 inclusion
NCBI: 6

* Exclusion

* Abstracts only:
Google Scholar: 1

Reviews:
Google Scholar: 1

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S. Wiklund	25/07/19		31/07/19	

Lifestyle

Title screening: Part 1
Inclusion
~~Search~~ Google scholar: 8
NCBI: 1

Exclusion:
Web of Science: 1
NCBI: 2
~~Not relevant~~
Not relevant
Scopus: 1
NCBI: 1
Google Scholar: 9

Part 2: Abstract screening
Inclusion
Google Scholar: 1

Exclusion
Glucuronides unreported
Google Scholar: 4
~~Disease~~ As

Disease not specified
Google Scholar: 1

Part 3: Inclusion
Google Scholar: 1

Performed by	Date	Countersigned by	Date	Continued on page number
J. Wadewal	25/07/19		31/07/19	

Breast cancer genetics

Part 1: Title screening

Inclusion
Scopus: 7
NCBI: 7

Exclusion
Duplicates
Web of Science: 4
NCBI: 5
Google scholar: 3

Not relevant
Scopus: 3
Web of Science: 2
NCBI: 2

No key words:
Scopus: 4
NCBI: 6
Google scholar: 3

Part 2: Abstract
Inclusion
Scopus: 6
NCBI: 1

*Exclusion
Neurovascular unreported
Scopus: 1
NCBI: 13

* Disease not specified
NCBI: 2

Part 3: Full paper
Inclusion: Scopus

Full exclusion:
full text unavailable:
Scopus: 1

Cell line studies:
Scopus: 1

Performed by	Date	Countersigned by	Date	Continued on page number
S. Weeland	25/07/19		31/07/19	

Liver cancer genetics

Part 1: Title screening

Inclusion
NCBI: 4
Google Scholar: 4

* Glucuronides reported that are not associated to disease:
Google scholar: 1

Exclusion:
Duplicates
NCBI: 6
Not relevant
Scopus: 16
Web of Science: 13
NCBI: 35
Google scholar: 10

keywords not specified
NCBI: 1

Part 2: Abstract screening
Inclusion
NCBI: 2
Google scholar: 1

Exclusion:
Glucuronides not reported
NCBI: 2
Google scholar: 3

*Part 3: Full paper analysis
Exclusion:
Cell line studies: 1

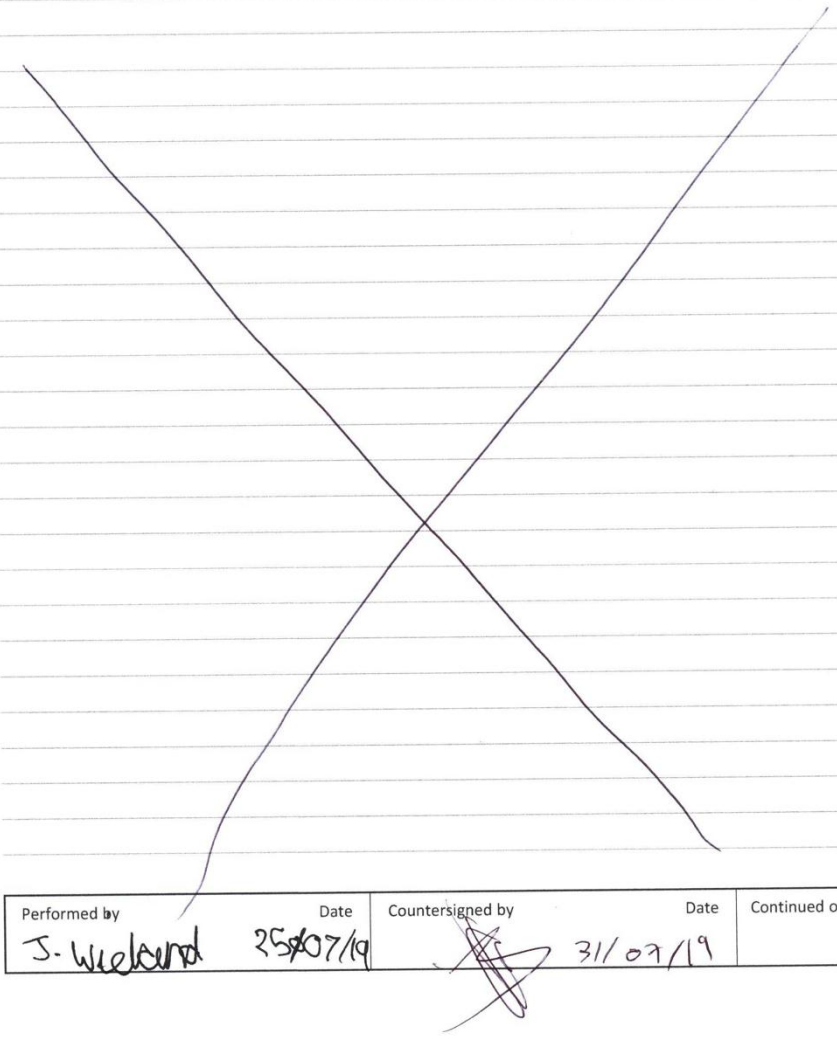
Performed by	Date	Countersigned by	Date	Continued on page number
J. Wieland	25/07/19		31/07/19	

Continued from page number | Page number 60

Lifestyle

Part 1: Title inclusion
Inclusion:
Google scholar: 1

Exclusion: (part 2 Abstract)
Glucuronides unreported
Google scholar: 1.



Performed by	Date	Countersigned by	Date	Continued on page number
J. Wiebeard	25/07/19		31/07/19	

Appendix 2: Inclusion and exclusion of retrieved articles

Colorectal cancer inclusion and exclusion

Genetics

Part 1: Title screening

Inclusion

Scopus

1. Labriet, A., De Mattia, E., Cecchin, E., et al., 2017. Improved progression-free survival in irinotecan-treated metastatic colorectal cancer patients carrying the HNF1A coding variant p.I27L. *Frontiers in Pharmacology* [online], 8 (712), doi: 10.3389/fphar.2017.00712.
2. Mbatchi, L. C., Robert, J., Ychou, M., et al., 2016. Effect of Single Nucleotide Polymorphisms in the Xenobiotic-sensing Receptors NR1I2 and NR1I3 on the Pharmacokinetics and Toxicity of Irinotecan in Colorectal Cancer Patients. *Clinical Pharmacokinetics* [online], 55 (9),1145 - 1157.
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5. Suenaga, M., Fuse, N., Yamaguchi, T., Yamanaka, Y., et al., 2014. Pharmacokinetics, safety, and efficacy of FOLFIRI plus bevacizumab in Japanese colorectal cancer patients with UGT1A1 gene polymorphisms. *Journal of Clinical Pharmacology* [online], 54 (5), 495 – 502.
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7. Park, S. R., Hong, Y. S., Lim, H-S., et al., 2013. Phase i clinical and pharmacokinetic/pharmacogenetic study of a triplet regimen of S-1/irinotecan/oxaliplatin in patients with metastatic colorectal or gastric cancer. *Cancer Chemotherapy and Pharmacology* [online], 72 (5), 953 – 964.
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1. Cai, X., Tian, C., Wang, L., et al., 2017. Correlative analysis of plasma SN-38 levels and DPD activity with outcomes of FOLFIRI regimen for metastatic colorectal cancer with UGT1A1 *28 and *6 wild type and its implication for individualized chemotherapy. Cancer Biology & Therapy [online], 18 (3),186 – 193.
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Exclusion

Duplicates

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1. Hazama, S., Nagashima, A., Kondo, H., et al., 2010. Phase I study of irinotecan and doxifluridine for metastatic colorectal cancer focusing on the UGT1A1*28 polymorphism. *Cancer Science* [online], 101 (3), 722 – 727.

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Not relevant

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1. Teft, W. A., Welch, S., Lenehan, J., et al., 2015. OATP1B1 and tumour OATP1B3 modulate exposure, toxicity, and survival after irinotecan-based chemotherapy. *British Journal of Cancer* [online], 112 (5), 857 – 865.
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1. De Mattia, E., Cecchin, E., Montico, M., et al., 2018. Association of STAT-3 rs1053004 and VDR rs11574077 With FOLFIRI-Related Gastrointestinal Toxicity in Metastatic Colorectal Cancer Patients. *Frontiers in Pharmacology* [online], 9 (367), doi: 10.3389/fphar.2018.00367.
2. Etienne-Grimadli, M. C., Boyer, J. C., Thomas, F., et al., 2015. UGT1A1 genotype and irinotecan therapy: general review and implementation in routine practice. *Fundamental & Clinical Pharmacology* [online], 29 (3), 219 – 237.
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Part 2: Abstract screening

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1. Snozek, C. L., O'Kane, D. J and Algeciras-Schimnich, A., 2009. Pharmacogenetics of solid tumors: directed therapy in breast, lung, and colorectal cancer: a paper from the 2008 william beaumont hospital symposium on molecular pathology. *The Journal of Molecular Diagnostics* [online], 11 (5), 381 – 389.
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Disease not specified

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1. Evrard, A and Mbatchi, L., 2012. Genetic polymorphisms of drug metabolizing enzymes and transporters: The long way from bench to bedside. Current Topics in Medicinal Chemistry [online], 12 (15), 1720 – 1729.
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3. Li, J and Bluth, M. H., 2011. Pharmacogenomics of drug metabolizing enzymes and transporters: Implications for cancer therapy. Pharmacogenomics and Personalized Medicine [online], 4 (1), 11 - 33.
4. Walko, C. M and McLeod, H., 2009. Pharmacogenomic progress in individualized dosing of key drugs for cancer patients. Nature Reviews Clinical Oncology [online], 6 (3), 153 – 162.
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Part 3: Full paper analysis

Inclusion

Scopus

1. Hazama, S., Nagashima, A., Kondo, H., et al., 2010. Phase I study of irinotecan and doxifluridine for metastatic colorectal cancer focusing on the UGT1A1*28 polymorphism. *Cancer Science* [online], 101 (3), 722 – 727.
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Exclusion

Abstract provided only

Scopus

1. Solier, S., Zhang, Y-W., Ballestrero, A., et al., 2012., DNA damage response pathways and cell cycle checkpoints in colorectal cancer: Current concepts and future perspectives for targeted treatment. Current Cancer Drug Targets, 12 (4), 356 - 371.
2. Maragon, E., Posocco, B., Mazzega, E., et al., 2015. Development and validation of a high-performance liquid chromatography-tandem mass

spectrometry method for the simultaneous determination of irinotecan and its main metabolites in human plasma and its application in a clinical pharmacokinetic study. *PLoS ONE* [online], 10 (2), e0118194.

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Web of Science

1. Liu, Y., Ramírez, J., House, L., et al., 2010. The UGT1A1*28 polymorphism correlates with erlotinib's effect on SN-38 glucuronidation. *European Journal of Cancer* [online], 46 (11), 2097 – 2103**.**
2. Hirose, K., Kozu, C., Yamashita, K., et al., 2012. Correlation between plasma concentration ratios of SN-38 glucuronide and sn-38 and neutropenia induction in patients with colorectal cancer and wild-type UGT1A1 gene. *Oncology Letters* [online], 3 (3), 694 – 698.
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Abstracts not provided

Google scholar

1. Liu, X and Xu, W., 2014. UGT1A1*28 polymorphisms: a potential pharmacological biomarker of irinotecan-based chemotherapies in colorectal cancer. *Pharmacogenomics* [online], 15 (9), 1171 – 1174.

Lifestyle

Part 1: Title screening

Inclusion

Scopus

1. Guertin, K. A., Moore, S. C., Sampson, J. N., et al., 2014. Metabolomics in nutritional epidemiology: Identifying metabolites associated with diet and quantifying their potential to uncover diet-disease relations in populations. *American Journal of Clinical Nutrition* [online], 100 (1), 208 – 217.
2. Deziel, N. C., Strickland, P. T., Platz, E. A., et al., 2011.Comparison of standard methods for assessing dietary intake of benzo[a]pyrene. *Cancer Epidemiology Biomarkers and Prevention* [online], 20 (5), 962 – 970.
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Understanding disease progression and what we can do to prevent it. *Cancers* [online], 10 (3), doi: 10.3390/cancers10030083.

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Google Scholar

1. Rossi, M., Jahanzaib Anwar, M., Usman A., et al., 2018. Colorectal Cancer and Alcohol Consumption-Populations to Molecules. *Cancers* [online],10 (2) doi: 10.3390/cancers10020038.
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3. Magalhães, B., Peleteiro, B and Lunet, N., 2012. Dietary patterns and colorectal cancer: systematic review and meta-analysis. *European Journal of Cancer Prevention* [online], 21 (1), 15 – 23.
4. Sakulterdkiat, T., Srisomsap, C., Udomsangpetch, R., et al., 2012. Curcumin Resistance Induced by Hypoxia in HepG2 Cells Is Mediated by Multidrug-resistance-associated Proteins. *Anticancer Research* [online], 32 (12), 5337 – 5342.
5. Andrea, A. Y., Berg, A., Zhu, J., et al., 2013. The effect of copy number variation in the phase II detoxification genes UGT2B17 and UGT2B28 on colorectal cancer risk. *Cancer* [online], 119 (13), 2477 – 2485.

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1. Falkowski, S., Woillard, J. B., Postil, D., et al., 2017. Common variants in glucuronidation enzymes and membrane transporters as potential risk factors for colorectal cancer: a case control study. *BMC Cancer* [online], 17 (1), doi: 10.1186/s12885-017-3728-0.

Excluded

Not relevant

Scopus

1. Kahle, K., Huemmer, W., Kempf, M., et al., 2007. Polyphenols are intensively metabolized in the human gastrointestinal tract after apple juice consumption. *Journal of Agricultural and Food Chemistry* [online], 55 (26), 10605 – 10614.
2. Cooke, D., Schwarz, M., Boocock, D., et al., 2006. Effect of cyanidin-3-glucoside and an anthocyanin mixture from bilberry on adenoma development in the ApcMin mouse model of intestinal carcinogenesis - Relationship with tissue anthocyanin levels. *International Journal of Cancer* [online], 119 (9), 2213 – 2220.
3. Kahle, K., Kraus, M., Scheppach, W., et al., 2005. Colonic availability of apple polyphenols--a study in ileostomy subjects. *Molecular Nutrition & Food Research* [online], 49 (12), 1143 – 1150.
4. Rafter, J., 2003. Probiotics and colon cancer. *Bailliere's Best Practice and Research in Clinical Gastroenterology* [online], 17 (5), 849 – 859.
5. Campbell, S., Stone, W., Whaley, S., et al., 2003. Development of gamma (γ)-tocopherol as a colorectal cancer chemopreventive agent. *Critical Reviews in Oncology/Hematology* [online], 47 (3), 249 – 259.

Part 2: Abstract screening

Inclusion

Scopus

1. Guertin, K. A., Moore, S. C., Sampson, J. N., et al., 2014. Metabolomics in nutritional epidemiology: Identifying metabolites associated with diet

and quantifying their potential to uncover diet-disease relations in populations. *American Journal of Clinical Nutrition* [online], 100 (1), 208 – 217.

2. Deziel, N. C., Strickland, P. T., Platz, E. A., et al., 2011.Comparison of standard methods for assessing dietary intake of benzo[a]pyrene. *Cancer Epidemiology Biomarkers and Prevention* [online], 20 (5), 962 – 970.
3. Hofmann, J. N., Liao, L. M., Strickland, P. T., et al., 2013. Polycyclic aromatic hydrocarbons: determinants of urinary 1-hydroxypyrene glucuronide concentration and risk of colorectal cancer in the Shanghai Women's Health Study. *BMC Cancer* [online], 13 (282). doi: 10.1186/1471-2407-13-282.

Exclusion

Glucuronides are not reported

Google scholar

1. Rossi, M., Jahanzaib Anwar, M., Usman A., et al., 2018. Colorectal Cancer and Alcohol Consumption-Populations to Molecules. *Cancers* [online],10 (2) doi: 10.3390/cancers10020038.
2. Magalhães, B., Peleteiro, B and Lunet, N., 2012. Dietary patterns and colorectal cancer: systematic review and meta-analysis. *European Journal of Cancer Prevention* [online], 21 (1), 15 – 23.

Part 3: Full paper analysis

Inclusion

Scopus

1. Guertin, K. A., Moore, S. C., Sampson, J. N., et al., 2014. Metabolomics in nutritional epidemiology: Identifying metabolites associated with diet and quantifying their potential to uncover diet-disease relations in populations. *American Journal of Clinical Nutrition* [online], 100 (1), 208 – 217.

Google Scholar

1. Hofmann, J. N., Liao, L. M., Strickland, P. T., et al., 2013. Polycyclic aromatic hydrocarbons: determinants of urinary 1-hydroxypyrene glucuronide concentration and risk of colorectal cancer in the Shanghai Women's Health Study. *BMC Cancer* [online], 13 (282). doi: 10.1186/1471-2407-13-282.

Exclusion

Disease unspecified

Scopus

1. Deziel, N. C., Strickland, P. T., Platz, E. A., et al., 2011.Comparison of standard methods for assessing dietary intake of benzo[a]pyrene. *Cancer Epidemiology Biomarkers and Prevention* [online], 20 (5), 962 – 970.

Type 2 Diabetes inclusion and exclusion

Genetics

Part 1: Title inclusion

Scopus

1. Khedher, B. M. R., Abid, M., Jamoussi, K., et al., 2018. Comprehensive insight into functional interaction between GNB3 C825T and eNOS T-786C, G894T gene polymorphisms and association with susceptibility to diabetic erectile dysfunction. Andrology [online], 6 (6), 865 – 873.
2. Mostafa-Hedeab, G., Mohamed, A. A., Ebid, G. T., et al., 2018. Effect of MATE 1, MATE 2 and OCT1 single nucleotide polymorphisms on metformin action in recently diagnosed egyptian type-2 diabetic patients. *Biomedical and Pharmacology Journal* [online], 11 (1), 149 – 157.
3. Raudenska, M., Dvorakova, V., Pacal, L., et al., 2017. Levels of heavy metals and their binding protein metallothionein in type 2 diabetics with kidney disease. *Journal of Biochemical and Molecular Toxicology* [online], 31 (6), e21891.
4. Dostalek, M., Court, M. H., Hazarika, S., et al., 2011. Diabetes mellitus reduces activity of human UDP-glucuronosyltransferase 2B7 in liver and kidney leading to decreased formation of mycophenolic acid acyl-glucuronide metabolite. Drug Metabolism and Disposition. 39 (3), 448 – 455.

Google scholar

1. Cheung, K. K-T., Lau, E. S., So, W. Y., et al., 2017. Low testosterone and clinical outcomes in Chinese men with type 2 diabetes mellitus – Hong Kong Diabetes Registry. Diabetes Research and Clinical Practice [online], 123, 97 – 105

Part 1 exclusion

Duplicates by title

Web of Science

1. Cheng, Y., Wang, L., Iacono, L., et al., 2018. Clinical significance of CYP2C19 polymorphisms on the metabolism and pharmacokinetics of 11β-hydroxysteroid dehydrogenase type-1 inhibitor BMS-823778. British Journal of Clinical Pharmacology [online], 84 (1), 130 - 141.
2. Jeong, H. U., Kim, J. H., Lee, D. Y., et al., 2015. In Vitro Metabolic Pathways of the New Anti-Diabetic Drug Evogliptin in Human Liver Preparations. Molecules [online], 20 (12), 21802 - 21815.
3. Su, H., Boulton, D. W., Barros, A., et al., 2012. Characterization of the in vitro and in vivo metabolism and disposition and cytochrome P450 inhibition/induction profile of saxagliptin in human. *Drug Metabolism & Disposition* [online], 40 (7), 1345 – 1356.

Not relevant

Scopus

1. Cheng, Y., Wang, L., Iacono, L., et al., 2018. Clinical significance of CYP2C19 polymorphisms on the metabolism and pharmacokinetics of 11β-hydroxysteroid dehydrogenase type-1 inhibitor BMS-823778. *British Journal of Clinical Pharmacology* [online], 84 (1), 130 – 141.
2. Jeong, H. U., Kim, J. H., Lee, D. Y., et al., 2015. In Vitro Metabolic Pathways of the New Anti-Diabetic Drug Evogliptin in Human Liver Preparations. *Molecules* [online], 20 (12), 21802 – 21815.
3. Su, H., Boulton, D. W., Barros, A., et al., 2012. Characterization of the in vitro and in vivo metabolism and disposition and cytochrome P450 inhibition/induction profile of saxagliptin in human. *Drug Metabolism and Disposition* [online], 40 (7), 1345 - 1356.
4. Itkonen, M. K., Tornio, A., Neuvonen, M., et al., 2016. Clopidogrel Markedly Increases Plasma Concentrations of CYP2C8 Substrate Pioglitazone. *Drug Metabolism and Disposition* [online], 44 (8), 1364 - 1371.

5. Su, H., Boulton, D. W., Barros, A., et al., 2012. Characterization of the in vitro and in vivo metabolism and disposition and cytochrome P450 inhibition/induction profile of saxagliptin in human. *Drug Metabolism and Disposition* [online], 40 (7), 1345 – 1356.

Web of Science

1. Abedelhedi, R., Kharrat, N., Maurer, M., et al., 2018. Impact of Clopidogrel Plasmatic Levels, CYP2C19 Polymorphisms and Drug-Drug Interactions on Clinical Outcome in Coronary Artery Disease Patients. *Farmacia* [online], 66, 135 – 148.

NCBI

1. Jeong, H. U., Kim, J. H., Lee, D. Y., et al., 2015. In Vitro Metabolic Pathways of the New Anti-Diabetic Drug Evogliptin in Human Liver Preparations. *Molecules* [online], 20 (12), 21802 - 21815.

Part 2: Abstract screening

Included

Scopus

1. Dostalek, M., Court, M. H., Hazarika, S., et al., 2011. Diabetes mellitus reduces activity of human UDP-glucuronosyltransferase 2B7 in liver and kidney leading to decreased formation of mycophenolic acid acyl-glucuronide metabolite. *Drug Metabolism and Disposition* [online]. 39 (3), 448 – 455.

Excluded

Glucuronide not reported

Scopus

1. Khedher, B. M. R., Abid, M., Jamoussi, K., et al., 2018. Comprehensive insight into functional interaction between GNB3 C825T and eNOS T-786C, G894T gene polymorphisms and association with susceptibility to diabetic erectile dysfunction. *Andrology* [online], 6 (6), 865 – 873.

2. Mostafa-Hedeab, G., Mohamed, A. A., Ebid, G. T., et al., 2018. Effect of MATE 1, MATE 2 and OCT1 single nucleotide polymorphisms on metformin action in recently diagnosed egyptian type-2 diabetic patients. *Biomedical and Pharmacology Journal* [online], 11 (1), 149 – 157.
3. Raudenska, M., Dvorakova, V., Pacal, L., et al., 2017. Levels of heavy metals and their binding protein metallothionein in type 2 diabetics with kidney disease. *Journal of Biochemical and Molecular Toxicology* [online], 31 (6), e21891.

Google scholar

1. Cheung, K. K-T., Lau, E. S., So, W. Y., et al., 2017. Low testosterone and clinical outcomes in Chinese men with type 2 diabetes mellitus – Hong Kong Diabetes Registry. Diabetes Research and Clinical Practice [online], 123, 97 – 105

Part 3: Full paper analysis

Excluded

Glucuronides reported that are not associated to disease

Scopus

1. Dostalek, M., Court, M. H., Hazarika, S., et al., 2011. Diabetes mellitus reduces activity of human UDP-glucuronosyltransferase 2B7 in liver and kidney leading to decreased formation of mycophenolic acid acyl-glucuronide metabolite. *Drug Metabolism and Disposition*. 39 (3), 448 – 455.

Lifestyle

Scopus

1. Li, J., Lai, H., Chen, S., et al., 2017. Interaction of sex steroid hormones and obesity on insulin resistance and type 2 diabetes in men: the Third National Health and Nutrition Examination Survey. Journal of Diabetes and its Complications [online], 31 (2), 318 – 327.

Google Scholar

1. Mora-Cubillos, X., Tulipani, S., Garcia-Aloy, M., et al., 2015. Plasma metabolomic biomarkers of mixed nuts exposure inversely correlate with severity of metabolic syndrome. Molecular Food Nutrition [online], 59 (12), 2480 – 2490.
2. Zhao. Q., Zhang, A., Zong, W., et al., 2017. Exploring potential biomarkers and determining the metabolic mechanism of type 2 diabetes mellitus using liquid chromatography coupled to high-resolution mass spectrometry. *RSC Advances* [online], 7, 44186 – 44198.

Part 1 exclusion

Duplicates by title

Scopus

1. Ji, L., Lai, H., Chen, S., et al., 2017. Interaction of sex steroid hormones and obesity on insulin resistance and type 2 diabetes in men: the Third National Health and Nutrition Examination Survey. Journal of Diabetes and its Complications [online], 31 (2), 318 – 327.

Web of Science

1. Ji, L., Lai, H., Chen, S., et al., 2017. Interaction of sex steroid hormones and obesity on insulin resistance and type 2 diabetes in men: the Third National Health and Nutrition Examination Survey. *Journal of Diabetes and its Complications* [online], 31 (2), 318 – 327.

NCBI

1. Brouwer-Brolsma, E. M., Brennan, L., Drevon, C. A., et al., 2017. Combining traditional dietary assessment methods with novel metabolomics techniques: present efforts by the Food Biomarker Alliance. Proceedings of the Nutrition Society [online], 76 (4), 619 – 627.

Not relevant

Web of Science

1. Anfossi, G., Frascaroli, C., Bonomo, K., et al., 2008. The NPC1L1 inhibitor ezetimibe in the treatment of the dyslipidemia in patients affected by the metabolic syndrome: Evidences and perspectives. *Current Enzyme Inhibition* [online], 4 (3), 109 – 120.

Part 2: Abstract analysis

Inclusion

Google scholar

1. Mora-Cubillos, X., Tulipani, S., Garcia-Aloy, M., et al., 2015. Plasma metabolomic biomarkers of mixed nuts exposure inversely correlate with severity of metabolic syndrome. Molecular Food Nutrition [online], 59 (12), 2480 – 2490.

Scopus

1. Li, J., Lai, H., Chen, S., et al., 2017. Interaction of sex steroid hormones and obesity on insulin resistance and type 2 diabetes in men: the Third National Health and Nutrition Examination Survey. *Journal of Diabetes and its Complications* [online], 31 (2), 318 – 327.
2. Sun, H., Zhang, S., Zhang, A., et al., 2014. Metabolomic analysis of diet-induced type 2 diabetes using UPLC/MS integrated with pattern recognition approach. *PLoS ONE* [online]. 9 (3), e93384.
3. Mora-Cubillos, X., Tulipani, S., Garcia-Aloy, M., et al., 2015. Plasma metabolomic biomarkers of mixed nuts exposure inversely correlate with

severity of metabolic syndrome. *Molecular Food Nutrition* [online], 59 (12), 2480 - 2490.

4. Guasch-Ferré, M., Merino, J., Sun, Q., et al., 2017. Dietary Polyphenols, Mediterranean Diet, Prediabetes, and Type 2 Diabetes: A Narrative Review of the Evidence. *Oxidative Medicine and Cellular Longevity* [online], doi: 10.1155/2017/6723931.

Part 3: Full paper analysis

Inclusion

Scopus

1. Li, J., Lai, H., Chen, S., et al., 2017. Interaction of sex steroid hormones and obesity on insulin resistance and type 2 diabetes in men: the Third National Health and Nutrition Examination Survey. *Journal of Diabetes and its Complications* [online], 31 (2), 318 – 327.

Google scholar

1. Zhao. Q., Zhang, A., Zong, W., et al., 2017. Exploring potential biomarkers and determining the metabolic mechanism of type 2 diabetes mellitus using liquid chromatography coupled to high-resolution mass spectrometry. RSC Advances [online], 7, 44186 – 44198.

Excluded

Glucuronides reported that do not come from human

Scopus

1. Sun, H., Zhang, S., Zhang, A., et al., 2014. Metabolomic analysis of diet-induced type 2 diabetes using UPLC/MS integrated with pattern recognition approach. *PLoS ONE* [online], 9 (3), e93384.

Google Scholar

1. Mora-Cubillos, X., Tulipani, S., Garcia-Aloy, M., et al., 2015. Plasma metabolomic biomarkers of mixed nuts exposure inversely correlate with severity of metabolic syndrome. *Molecular Food Nutrition* [online], 59 (12), 2480 - 2490.

Reviews (Literature/systematic)

Scopus

1. Guasch-Ferré, M., Merino, J., Sun, Q., et al., 2017. Dietary Polyphenols, Mediterranean Diet, Prediabetes, and Type 2 Diabetes: A Narrative Review of the Evidence. *Oxidative Medicine and Cellular Longevity* [online], doi: 10.1155/2017/6723931.

Parkinson’s disease inclusion and exclusion

Genetics

Part 1: Title screening

Scopus

1. Leuratti, C., Sardina, M., Ventura, P., et al., 2013. Disposition and metabolism of safinamide, a novel drug for Parkinson's disease, in healthy male volunteers. *Pharmacology* [online], 92 (3-4), 207 – 216.

Exclusion

Duplicates by title

Web of Science

1. Nakajima, M and Yokoi, T., 2005. Interindividual variability in nicotine metabolism: C-oxidation and glucuronidation. *Drug Metabolism and Pharmacokinetics* [online], 20 (4), 227 – 235.

Not relevant

Scopus

1. Nakajima, M and Yokoi, T., 2005. Interindividual variability in nicotine metabolism: C-oxidation and glucuronidation. *Drug Metabolism and Pharmacokinetics* [online], 20 (4), 227 – 235.

Web of Science

1. Almeida, L., Loureiro, A. I., Vaz-da-Silva, M., et al., 2010. Chronopharmacology of nebicapone, a new catechol-O-methyltransferase inhibitor. *Current Medical Research and Opinion* [online], 1097 – 1108.
2. Hajihashemi, S and Geuns, J. M. X., 2013. Radical scavenging activity of steviol glycosides, steviol glucuronide and crude Stevia extracts. *Free Radicals and Antioxidants* [online], 3 (2), 34 – 39.
3. Laux-Biechlmann, A., Mouheiche, J., Veriepe, J., et al., 2013. Endogenous morphine and its metabolites in mammals: history,

synthesis, localization and perspectives. *Neuroscience* [online], 233, 95 – 117.

4. Gallardo, E., Sarriá, B., Espartero, J. L., et al., 2016. Evaluation of the Bioavailability and Metabolism of Nitroderivatives of Hydroxytyrosol Using Caco-2 and HepG2 Human Cell Models. *Journal of Agricultural and Food Chemistry* [online], 64 (11), 2289 – 2297.

NCBI

1. Martignoni, E., Cosentino, M., Ferrari, M., et al., 2005. Two patients with COMT inhibitor-induced hepatic dysfunction and UGT1A9 genetic polymorphism. *Neurology* [online], 65 (11), 1820 – 1822.

Part 2: Abstract screening

Excluded

Glucuronides not reported

1. Leuratti, C., Sardina, M., Ventura, P., et al., 2013. Disposition and metabolism of safinamide, a novel drug for Parkinson's disease, in healthy male volunteers. *Pharmacology* [online], 92 (3-4), 207 – 216.

Lifestyle

Part 1: Title screening

Exclusion

Duplicates by title

Web of Science

1. Almeida, L., Loureiro, A. I., Vaz-da-Silva, M., et al., 2010. Chronopharmacology of nebicapone, a new catechol-O-methyltransferase inhibitor. *Current Medical Research and Opinion* [online], 1097 – 1108.
2. Hajihashemi, S and Geuns, J. M. X., 2013. Radical scavenging activity of steviol glycosides, steviol glucuronide and crude Stevia extracts. *Free Radicals and Antioxidants* [online], 3 (2), 34 – 39.

3. Leuratti, C., Sardina, M., Ventura, P., et al., 2013. Disposition and metabolism of safinamide, a novel drug for Parkinson's disease, in healthy male volunteers. *Pharmacology* [online], 92 (3-4), 207 – 216.
4. Laux-Biechlmann, A., Mouheiche, J., et al., 2013. Endogenous morphine and its metabolites in mammals: history, synthesis, localization and perspectives. *Neuroscience* [online], 233, 95 – 117.

Not relevant

Web of Science

1. Angeloni, C., Malaguti, M., Barbalace, M. C., et al., 2017. Bioactivity of olive oil phenols in neuroprotection. *International Journal of Molecular Sciences* [online], 18 (11), doi: 10.3390/ijms18112230.
2. Speciale, A., Chirafisi, J., Saija, A., et al., 2011. Nutritional antioxidants and adaptive cell responses: An update. *Current Molecular Medicine* [online], 11 (9), 770 – 789.
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Prostate cancer inclusion and exclusion

Genetics

Part 1:

Inclusion

NCBI

1. Grant, D. J., Hoyo, C., Oliver, S. D., et al., 2013. Association of uridine diphosphate-glucuronosyltransferase 2B gene variants with serum glucuronide levels and prostate cancer risk. *Genetic Testing and Molecular Biomarkers* [online], 17 (1), 3 – 9.
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5. Karatzas, A., Giannatou, E., Tzortzis, V., et al., 2010. Genetic polymorphisms in the UDP-glucuronosyltransferase 1A1 (UGT1A1) gene and prostate cancer risk in Caucasian men. *Cancer Epidemiology* [online], 34 (3), 345 – 349.
6. Hu, D. G, Gardner-Stephen, D., Severi, G., et al, 2010. A novel polymorphism in a forkhead box A1 (FOXA1) binding site of the human UDP glucuronosyltransferase 2B17 gene modulates promoter activity and is associated with altered levels of circulating androstane-3α,17β-diol glucuronide. *Molecular Pharmacology* [online], 78 (4), 714 – 722.
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prostate, lung, colorectal, and ovarian study. *Prostate* [online], 72 (1), 65 – 71.

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Google scholar

1. Grant, D. J., Hoyo, C., Oliver, S. D., et al., 2013. Association of uridine diphosphate glucuronosyltransferase 2B gene variants with serum glucuronide levels and prostate cancer risk. Genetic Testing and Molecular Biomarkers [online], 17 (1), 3 – 9.
2. Karatzas, A., Giannatou, E., Tzortzis, V., et al., 2010. Genetic polymorphisms in the UDP-glucuronosyltransferase 1A1 (UGT1A1) gene and prostate cancer risk in Caucasian men. *Cancer Epidemiology* [online], 34 (3), 345 – 349.
3. Gauthier-Landry, L., Bélanger, A and Barbier, O., 2015. Multiple roles for UDP-glucuronosyltransferase (UGT)2B15 and UGT2B17 enzymes in androgen metabolism and prostate cancer evolution. *The Journal of Steroid Biochemistry and Molecular Biology* [online], 145, 187 – 192.
4. Mononen, N and Schleutker, J., 2009. Polymorphisms in genes involved in androgen pathways as risk factors for prostate cancer. *The Journal of Urology* [online], 181 (4), 1541 – 1549.
5. Setlur, S. R., Chen, C. X., Hossain, R. R., et al., 2010. Genetic variation of genes involved in dihydrotestosterone metabolism and the risk of prostate cancer. *Cancer Epidemiology, Biomarkers & Prevention* [online], 19 (1), 229 – 239.

6. McNamara, K. M., Nakamura, Y., Miki, Y., et al., 2013. Phase two steroid metabolism and its roles in breast and prostate cancer patients. *Frontiers in Endocrinology* [online], 4 (116), doi: 10.3389/fendo.2013.00116.
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10. Travis, R. C., Key, T. J., Allen, N. E., et al., 2007. Serum androgens and prostate cancer among 643 cases and 643 controls in the European Prospective Investigation into Cancer and Nutrition. *International Journal of Cancer* [online], 121 (6), 1331 – 1338.

Exclusion

Part 1:

Not relevant

Scopus

1. Weisenburger, J. H and Chung, F-L., 2002. Mechanisms of chronic disease causation by nutritional factors and tobacco products and their prevention by tea polyphenols. *Food and Chemical Toxicology* [online], 40 (8), 1145 – 1154.

NCBI

1. Church, T. R., Haznadar, M., Geisser, M. S., et al., 2010. Interaction of CYP1B1, cigarette-smoke carcinogen metabolism, and lung cancer risk.

International Journal of Molecular Epidemiology and Genetics [online], 1 (4), 295 – 309.

2. Bushey, R. T., Chen, G., Blevins-Primeau, A. S., et al., 2011. Characterization of UDP-glucuronosyltransferase 2A1 (UGT2A1) variants and their potential role in tobacco carcinogenesis. *Pharmacogenetics and Genomics* [online], 21 (2), 55 – 65.
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The Journal of Clinical Endocrinology and Metabolism [online], 91 (2), 687 – 693.

Duplicates by title

Web of Science

1. Weisenburger, J. H and Chung, F-L., 2002. Mechanisms of chronic disease causation by nutritional factors and tobacco products and their prevention by tea polyphenols. Food and Chemical Toxicology [online], 40 (8), 1145 – 1154.

NCBI

1. Gallagher, C. J., Kadlubar, F. F., Muscat, J. E., et al., 2007. The UGT2B17 gene deletion polymorphism and risk of prostate cancer. A case-control study in Caucasians. *Cancer Detection and Prevention* [online], 31 (4), 310 – 315.
2. Allen, N. E., Reichardt, J. K., Nguyen, H., et al., 2003. Association between two polymorphisms in the SRD5A2 gene and serum androgen concentrations in British men. *Cancer Epidemiology, Biomarkers & Prevention* [online], 12 (6), 578 – 581.
3. Allen, N. E., Forrest, M. S and Key, T. J., 2001. The association between polymorphisms in the CYP17 and 5alpha-reductase (SRD5A2) genes and serum androgen concentrations in men. *Cancer Epidemiology, Biomarkers & Prevention* [online], 185 – 189.
4. Wang, Y and Zheng, Y., 2008. Review on gene polymorphisms of UDP-glucuronosyltransferases and genetic susceptibility of cancer. *Wei Sheng Yan Jiu* (*Journal of Hygiene Research)* [online], 37 (5), 629 – 632.
5. Macleod, S. L., Nowell, S., Plaxco, J., et al., 2000. An allele-specific polymerase chain reaction method for the determination of the D85Y polymorphism in the human UDP-glucuronosyltransferase 2B15 gene in a case-control study of prostate cancer. *Annals of Surgical Oncology* [online], 7 (10), 777 – 782.

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1. Gallagher, C. J., Kadlubar, F. F., Muscat, J. E., et al., 2007. The UGT2B17 gene deletion polymorphism and risk of prostate cancer. A case-control study in Caucasians. Cancer Detection and Prevention [online], 31 (4), 310 – 315.
2. Park, J., Chen, L., Ratnashinge, L., et al., 2006. Deletion polymorphism of UDP-glucuronosyltransferase 2B17 and risk of prostate cancer in African American and Caucasian men. *Cancer Epidemiology, Biomarkers & Prevention* [online], 15 (8), 1473 – 1478.
3. Gallagher, C. J., Kadlubar, F. F., Muscat, J. E., et al., 2007. The UGT2B17 gene deletion polymorphism and risk of prostate cancer. A case-control study in Caucasians. *Cancer Detection and Prevention* [online], 31 (4), 310 – 315.
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5. Chu, L. W., Zhu, Y., Yu, K., et al., 2008. Correlation between circadian gene variants and serum levels of sex steroids and insulin-like growth factor-I. Cancer Epidemiology, Biomarkers & Prevention [online], 17 (11), 3268 – 3273.
6. Singh, P. B., Matanhelia, S. S and Martin, F. L., 2008. A potential paradox in prostate adenocarcinoma progression: oestrogen as the initiating driver. *European Journal of Cancer* [online], 44 (7), 928 – 936.
7. Travis, R. C., Key, T. J., Allen, N. E., et al., 2007. Serum androgens and prostate cancer among 643 cases and 643 controls in the European Prospective Investigation into Cancer and Nutrition. *International Journal of Cancer* [online], 121 (6), 1331 – 1338.

Part 2 abstract analysis:

Inclusion:

NCBI

1. Grant, D. J., Hoyo, C., Oliver, S. D., et al., 2013. Association of uridine diphosphate-glucuronosyltransferase 2B gene variants with serum glucuronide levels and prostate cancer risk. *Genetic Testing and Molecular Biomarkers* [online], 17 (1), 3 – 9.
2. Lévesque, É., Laverdière, I., Lacombe, L., et al., 2014. Importance of 5α-reductase gene polymorphisms on circulating and intraprostatic androgens in prostate cancer. *Clinical Cancer Research* [online], 20 (3), 576 – 584.
3. Nadeau, G., Bellemare, J., Audet-Walsh, É., et al., 2011. Deletions of the androgen-metabolizing UGT2B genes have an effect on circulating steroid levels and biochemical recurrence after radical prostatectomy in localized prostate cancer. *The Journal of Clinical Endocrinology and Metabolism* [online], 96 (9), 1550 – 1557.
4. Hsing, A. W., Chen, C., Chokkalingam, A. P., et al., 2001. Polymorphic markers in the SRD5A2 gene and prostate cancer risk: a population-based case-control study. *Cancer Epidemiology, Biomarkers & Prevention* [online], 10 (10), 1077 – 1082.
5. Macleod, S. L., Nowell, S., Plaxco, J., et al., 2000. An allele-specific polymerase chain reaction method for the determination of the D85Y polymorphism in the human UDP-glucuronosyltransferase 2B15 gene in a case-control study of prostate cancer. *Annals of Surgical Oncology* [online], 7 (10), 777 – 782.
6. Eaton, N. E., Reeves, G. K., Appleby, P. N., et al., 1999. Endogenous sex hormones and prostate cancer: a quantitative review of prospective studies. *British Journal of Cancer* [online], 80 (7), 930 – 934.

Google scholar

1. Gauthier-Landry, L., Bélanger, A and Barbier, O., 2015. Multiple roles for UDP-glucuronosyltransferase (UGT)2B15 and UGT2B17 enzymes in

androgen metabolism and prostate cancer evolution. *The Journal of Steroid Biochemistry and Molecular Biology* [online], 145, 187 – 192.

2. Setlur, S. R., Chen, C. X., Hossain, R. R., et al., 2010. Genetic variation of genes involved in dihydrotestosterone metabolism and the risk of prostate cancer. Cancer Epidemiology, Biomarkers & Prevention [online], 19 (1), 229 – 239.

Exclusion:

Glucuronides unreported

NCBI

1. Hu, D. G., Mackenzie, P. I., McKinnon, R. A., et al., 2016. Genetic polymorphisms of human UDP-glucuronosyltransferase (UGT) genes and cancer risk. *Drug Metabolism Reviews* [online], 48 (1), 47 – 69.
2. Karatzas, A., Giannatou, E., Tzortzis, V., et al., 2010. Genetic polymorphisms in the UDP-glucuronosyltransferase 1A1 (UGT1A1) gene and prostate cancer risk in Caucasian men. *Cancer Epidemiology* [online], 34 (3), 345 – 349.
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4. Meyer, T. E., Chu, L. W., Li, Q., et al., 2012. The association between inflammation-related genes and serum androgen levels in men: the prostate, lung, colorectal, and ovarian study. *Prostate* [online], 72 (1), 65 – 71.
5. Park, J., Chen, L., Ratnashinge, L., et al., 2006. Deletion polymorphism of UDP-glucuronosyltransferase 2B17 and risk of prostate cancer in African American and Caucasian men. *Cancer Epidemiology, Biomarkers & Prevention* [online], 15 (8), 1473 – 1478.
6. Gallagher, C. J., Kadlubar, F. F., Muscat, J. E., et al., 2007. The UGT2B17 gene deletion polymorphism and risk of prostate cancer. A case-control study in Caucasians. *Cancer Detection and Prevention* [online], 31 (4), 310 – 315.

Google scholar

1. Karatzas, A., Giannatou, E., Tzortzis, V., et al., 2010. Genetic polymorphisms in the UDP-glucuronosyltransferase 1A1 (UGT1A1) gene and prostate cancer risk in Caucasian men. *Cancer Epidemiology* [online], 34 (3), 345 – 349.
2. Mononen, N and Schleutker, J., 2009. Polymorphisms in genes involved in androgen pathways as risk factors for prostate cancer. *The Journal of Urology* [online], 181 (4), 1541 – 1549.
3. McNamara, K. M., Nakamura, Y., Miki, Y., et al., 2013. Phase two steroid metabolism and its roles in breast and prostate cancer patients. *Frontiers in Endocrinology* [online], 4 (116), doi: 10.3389/fendo.2013.00116.
4. Fujimoto, N., Kubo, T., Inatomi, H., et al., 2013. Polymorphisms of the androgen transporting gene SLCO2B1 may influence the castration resistance of prostate cancer and the racial differences in response to androgen deprivation. *Prostate Cancer and Prostatic Diseases* [online], 16 (4), 336 – 340.
5. Vidal, A. C., Tucker, C., Schlidkraut, J. M., et al., 2013. Novel associations of UDP-glucuronosyltransferase 2B gene variants with prostate cancer risk in a multiethnic study. BMC Cancer [online], 13 (556), doi: 10.1186/1471-2407-13-556.

Part 3 inclusion

NCBI

1. Grant, D. J., Hoyo, C., Oliver, S. D., et al., 2013. Association of uridine diphosphate-glucuronosyltransferase 2B gene variants with serum glucuronide levels and prostate cancer risk. *Genetic Testing and Molecular Biomarkers* [online], 17 (1), 3 – 9.
2. Lévesque, É., Laverdière, I., Lacombe, L., et al., 2014. Importance of 5α-reductase gene polymorphisms on circulating and intraprostatic androgens in prostate cancer. *Clinical Cancer Research* [online], 20 (3), 576 – 584.
3. Nadeau, G., Bellemare, J., Audet-Walsh, É., et al., 2011. Deletions of the androgen-metabolizing UGT2B genes have an effect on circulating

steroid levels and biochemical recurrence after radical prostatectomy in localized prostate cancer. *The Journal of Clinical Endocrinology and Metabolism* [online], 96 (9), 1550 – 1557.

4. Hsing, A. W., Chen, C., Chokkalingam, A. P., et al., 2001. Polymorphic markers in the SRD5A2 gene and prostate cancer risk: a population-based case-control study. *Cancer Epidemiology, Biomarkers & Prevention* [online], 10 (10), 1077 – 1082.

Exclusion

Abstract provided only:

Google Scholar

1. Gauthier-Landry, L., Bélanger, A and Barbier, O., 2015. Multiple roles for UDP-glucuronosyltransferase (UGT)2B15 and UGT2B17 enzymes in androgen metabolism and prostate cancer evolution. *The Journal of Steroid Biochemistry and Molecular Biology* [online], 145, 187 – 192.

Reviews (Literature/systematic)

1. Eaton, N. E., Reeves, G. K., Appleby, P. N., et al., 1999. Endogenous sex hormones and prostate cancer: a quantitative review of prospective studies. *British Journal of Cancer* [online], 80 (7), 930 – 934.

Lifestyle

Part 1: Title screening

Inclusion

Google scholar

1. Suzuki, R., Allen, N. E., Appleby, P. N., et al., 2009. Lifestyle factors and serum androgens among 636 middle aged men from seven countries in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Cancer Causes & Control* [online], 20 (6), 811 – 821.
2. DeVere White, R. W., Tsodikov, A., Stapp, E. C., et al., 2010. Effects of a high dose, aglycone-rich soy extract on prostate-specific antigen and serum isoflavone concentrations in men with localized prostate cancer. *Nutrition and Cancer* [online], 62 (8), 1036 – 1043.
3. Liao, C. H., Li, H. Y., Chung, S. D., et al., 2012. Significant association between serum dihydrotestosterone level and prostate volume among Taiwanese men aged 40-79 years. *The Aging Male* [online], 15 (1), 28 – 33.
4. Grainger, E. M., Moran, N. E., Francis, D. M., et al., 2018. A novel tomato-soy juice induces a dose-response increase in urinary and plasma phytochemical biomarkers in men with prostate cancer. *The Journal of Nutrition* [online], 149 (1), 26 – 35.
5. Arthur. R., Rohrmann, S., Møller, H., et al., 2017. Pre-diabetes and serum sex steroid hormones among US men. *Andrology* [online], 5 (1), 49 – 57.
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prostate cancer. *Cancer Epidemiology, Biomarkers & Prevention* [online], 19 (1), 229 – 239.

NCBI

1. Arthur. R., Rohrmann, S., Møller, H., et al., 2017. Pre-diabetes and serum sex steroid hormones among US men. *Andrology* [online], 5 (1), 49 – 57.

Exclusion

Duplicates

Web of Science

1. Weisenburger, J. H and Chung, F-L., 2002. Mechanisms of chronic disease causation by nutritional factors and tobacco products and their prevention by tea polyphenols. *Food and Chemical Toxicology* [online], 40 (8), 1145 – 1154.

NCBI

1. Weisenburger, J. H and Chung, F-L., 2002. Mechanisms of chronic disease causation by nutritional factors and tobacco products and their prevention by tea polyphenols. *Food and Chemical Toxicology* [online], 40 (8), 1145 – 1154.
2. Grant, D. J., Hoyo, C., Oliver, S. D., et al., 2013. Association of uridine diphosphate-glucuronosyltransferase 2B gene variants with serum glucuronide levels and prostate cancer risk. Genetic Testing and Molecular Biomarkers [online], 17 (1), 3 – 9.

Not relevant

Scopus

1. Weisenburger, J. H and Chung, F-L., 2002. Mechanisms of chronic disease causation by nutritional factors and tobacco products and their prevention by tea polyphenols. *Food and Chemical Toxicology* [online], 40 (8), 1145 – 1154.

NCBI

1. Wu, A. H., Whittemore, A. S., Kolonel, L. N., et al., 2001. Lifestyle determinants of 5alpha-reductase metabolites in older African-American, white, and Asian-American men. *Cancer Epidemiology, Biomarkers & Prevention* [online], 10 (5), 533 – 538.

Google scholar

1. Platz, E. A., Rimm, E. B., Willet, W. C., et al., 2000. Racial variation in prostate cancer incidence and in hormonal system markers among male health professionals. *Journal of the National Cancer Institute* [online], 92 (24), 2009 – 2017.
2. Travis, R. C., Key, T. J., Allen, N. E., et al., 2007. Serum androgens and prostate cancer among 643 cases and 643 controls in the European Prospective Investigation into Cancer and Nutrition. International Journal of Cancer [online], 121 (6), 1331 – 1338.
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5. Nan, H. M., Kim, H., Lim, H. S., et al., 2001. Effects of occupation, lifestyle and genetic polymorphisms of CYP1A1, CYP2E1, GSTM1 and GSTT1 on urinary 1-hydroxypyrene and 2-naphthol concentrations. *Carcinogenesis* [online], 22 (5), 787 – 793.
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7. Mohr, B. A., Feldman, H. A., Kalish, L. A., et al., 2001. Are serum hormones associated with the risk of prostate cancer? Prospective results from the Massachusetts Male Aging Study. *Urology* [online], 57 (5), 930 – 935.

8. Wang, C., Christenson, P and Swerdloff, R., 2007. Clinical Relevance of Racial and Ethnic Differences in Sex Steroids. *The Journal of Clinical Endocrinology & Metabolism* [online], 92 (7), 2433 – 2435.
9. Marks, L. S., Hess, D. L., Dorey, F. J., et al., 2006. Prostatic tissue testosterone and dihydrotestosterone in African-American and white men. *Urology* [online], 68 (2), 337 – 341.

Part 2: Abstract screening

Inclusion

Google Scholar

1. Suzuki, R., Allen, N. E., Appleby, P. N., et al., 2009. Lifestyle factors and serum androgens among 636 middle aged men from seven countries in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Cancer Causes & Control* [online], 20 (6), 811 – 821.

Exclusion

Glucuronides unreported

Google Scholar

1. Arthur. R., Rohrmann, S., Møller, H., et al., 2017. Pre-diabetes and serum sex steroid hormones among US men. *Andrology* [online], 5 (1), 49 – 57.
2. DeVere White, R. W., Tsodikov, A., et al., 2010. Effects of a high dose, aglycone-rich soy extract on prostate-specific antigen and serum isoflavone concentrations in men with localized prostate cancer. *Nutrition and Cancer* [online], 62 (8), 1036 – 1043.
3. Grainger, E. M., Moran, N. E., Francis, D. M., et al., 2018. A novel tomato-soy juice induces a dose-response increase in urinary and plasma phytochemical biomarkers in men with prostate cancer. *The Journal of Nutrition* [online], 149 (1), 26 – 35.
4. Setlur, S. R., Chen, C. X., Hossain, R. R., et al., 2010. Genetic variation of genes involved in dihydrotestosterone metabolism and the risk of

prostate cancer. *Cancer Epidemiology, Biomarkers & Prevention* [online], 19 (1), 229 – 239.

Disease not specified

Google Scholar

1. Liao, C. H., Li, H. Y., Chung, S. D., et al., 2012. Significant association between serum dihydrotestosterone level and prostate volume among Taiwanese men aged 40-79 years. *The Aging Male* [online], 15 (1), 28 – 33.

Part 3: Inclusion

Google Scholar

1. Suzuki, R., Allen, N. E., Appleby, P. N., et al., 2009. Lifestyle factors and serum androgens among 636 middle aged men from seven countries in the European Prospective Investigation into Cancer and Nutrition (EPIC). *Cancer Causes & Control* [online], 20 (6), 811 – 821.

Breast cancer inclusion and exclusion

Genetics

Part 1: Title screening

Inclusion

Scopus

1. Johnson, N., De Ieso, P., et al., 2016. Cytochrome P450 allele CYP3A7*1C associates with adverse outcomes in chronic lymphocytic Leukemia, Breast, and Lung Cancer. *Cancer Research* [online], 76 (6), 1485 – 1493.
2. Romero-Lorca, A., Novillo, A., Gaibar, M., et al., 2015. Impacts of the glucuronidase genotypes UGT1A4, UGT2B7, UGT2B15 and UGT2B17 on tamoxifen metabolism in breast cancer patients. *PLoS ONE* [online], 10 (7), e0132269.
3. Johnson, N., Walker, K., Gibson, L.J., et al., 2012. CYP3A variation, premenopausal estrone levels, and breast cancer risk. *Journal of the National Cancer Institute* [online], 104 (9), 657 – 669.
4. Figueroa, J. D and Brinton, L. A., 2012. Unraveling genes, hormones, and breast cancer. *Journal of the National Cancer Institute* [online], 104 (9), 641 – 642.
5. Mürdter, T. E., Schroth, W., Bacchus-Gerybadze, L., et al., 2011. Activity levels of tamoxifen metabolites at the estrogen receptor and the impact of genetic polymorphisms of phase i and II enzymes on their concentration levels in plasma. *Clinical Pharmacology and Therapeutics* [online], 89 (5), 1 – 10.
6. Sun, D., Chen, G., Dellinger, R. W., et al., 2010. Characterization of 17-dihydroexemestane glucuronidation: Potential role of the UGT2B17 deletion in exemestane pharmacogenetics. *Pharmacogenetics and Genomics* [online], 20 (10), 575 – 585.
7. Sutiman, N., Lim, J. S. L., Muerdter, T. E., et al., 2016. Pharmacogenetics of UGT1A4, UGT2B7 and UGT2B15 and Their Influence on Tamoxifen Disposition in Asian Breast Cancer Patients. *Clinical Pharmacokinetics* [online], 55 (10), 1239 – 1250.

NCBI

1. Hu, D. G., Mackenzie, P. I., McKinnon, R. A., et al., 2013. Genetic polymorphisms of human UDP-glucuronosyltransferase (UGT) genes and cancer risk. *Drug Metabolism Reviews* [online], 48 (1), 47 – 69.
2. Johnson, N., Dudbridge, F., Orr, N., et al., 2014. Genetic variation at CYP3A is associated with age at menarche and breast cancer risk: a case-control study. *Breast Cancer Research* [online], 16 (3), doi: 10.1186/bcr3662.
3. Johnson, N., Walker, K., Gibson, L. J., et al., 2012. CYP3A variation, premenopausal estrone levels, and breast cancer risk. *Journal of the National Cancer Institute* [online], 104 (9), 657 – 659.
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7. Wang, Y and Zhen, Y., 2008. Review on gene polymorphisms of UDP-glucuronosyltransferases and genetic susceptibility of cancer. *Wei Sheng Yan Jiu* (*Journal of Hygiene Research*), 37 (5), 629 – 632.

Exclusion

Duplicates by title

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1. Romero-Lorca, A., Novillo, A., Gaibar, M., et al., 2015. Impacts of the glucuronidase genotypes UGT1A4, UGT2B7, UGT2B15 and UGT2B17 on tamoxifen metabolism in breast cancer patients. *PLoS ONE* [online], 10 (7), e0132269.
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Part 2 abstract screening

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1. Johnson, N., De Ieso, P., Migliorini, G., Orr, N., et al., 2016. Cytochrome P450 allele CYP3A7*1C associates with adverse outcomes in chronic lymphocytic Leukemia, Breast, and Lung Cancer. *Cancer Research* [online], 76 (6), 1485 – 1493.
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Exclusion

Glucuronides not reported

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Part 3:Full paper screening

Inclusion

Scopus

1. Johnson, N., De Ieso, P., Migliorini, G., et al., 2016. Cytochrome P450 allele CYP3A7*1C associates with adverse outcomes in chronic lymphocytic Leukemia, Breast, and Lung Cancer. *Cancer Research* [online], 76 (6), 1485 – 1493.
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Lifestyle

Part 1: Title screening

Inclusion

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1. Yong, M., Schwartz, S. M., Atkinson, C., et al., 2010. Associations between polymorphisms in glucuronidation and sulfation enzymes and mammographic breast density in premenopausal women in the United States. *Cancer Epidemiology, Biomarkers and Prevention* [online], 19 (2), 537 – 546.
2. Ávila-Gálves, M. Á., Espín, J. C and González-Sarrías, A., 2018. Physiological Relevance of the Antiproliferative and Estrogenic Effects of Dietary Polyphenol Aglycones versus Their Phase-II Metabolites on Breast Cancer Cells: A Call of Caution. *Journal of Agriculture and Food Chemistry* [online], 66 (32), 8547 – 8555.
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Exclusion

Duplicates by title

Web of Science

1. Weisburger, J. H and Chung, F-L., 2002. Mechanisms of chronic disease causation by nutritional factors and tobacco products and their prevention by tea polyphenols. *Food and Chemical Toxicology* [online], 40 (8), 1145 – 1154.

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prevention by tea polyphenols. *Food and Chemical Toxicology* [online], 40 (8), 1145 – 1154.

2. Johnson, N., Walker, K., Gibson, L.J., et al., 2012. CYP3A variation, premenopausal estrone levels, and breast cancer risk. *Journal of the National Cancer Institute* [online], 104 (9), 657 – 669.

Not relevant

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Part 2: Abstract screening

Inclusion

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Exclusion

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1. Armitage, E. G and Barbas, C., 2014. Metabolomics in cancer biomarker discovery: current trends and future perspectives. *Journal of Pharmaceutical and Biomedical Analysis* [online], 87, 1 – 11.

Disease not specified

NCBI

1. Yong, M., Schwartz, S. M., Atkinson, C., et al., 2010. Associations between polymorphisms in glucuronidation and sulfation enzymes and mammographic breast density in premenopausal women in the United States. *Cancer Epidemiology, Biomarkers and Prevention* [online], 19 (2), 537 – 546.

Part 3: Full paper analysis

Excluded:

Abstract provided only:

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1. Ávila-Gálves, M. Á., Espín, J. C and González-Sarrías, A., 2018. Physiological Relevance of the Antiproliferative and Estrogenic Effects of Dietary Polyphenol Aglycones versus Their Phase-II Metabolites on Breast Cancer Cells: A Call of Caution. *Journal of Agriculture and Food Chemistry* [online], 66 (32), 8547 – 8555.

Liver cancer inclusion and exclusion

Genetics

Part 1: Title screening

Inclusion

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Keyword(s) not specified

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Part 2: Abstract screening

Inclusion

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Exclusion

Glucuronides not reported

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Part 3: Full paper analysis

Exclusion

Cell line studies

NCBI

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Glucuronides reported that are not associated to disease

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Lifestyle

Part 1: Title screening

Inclusion

Google Scholar

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Exclusion

Not relevant

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Part 2: Abstract

Excluded

Glucuronides not reported

Google Scholar

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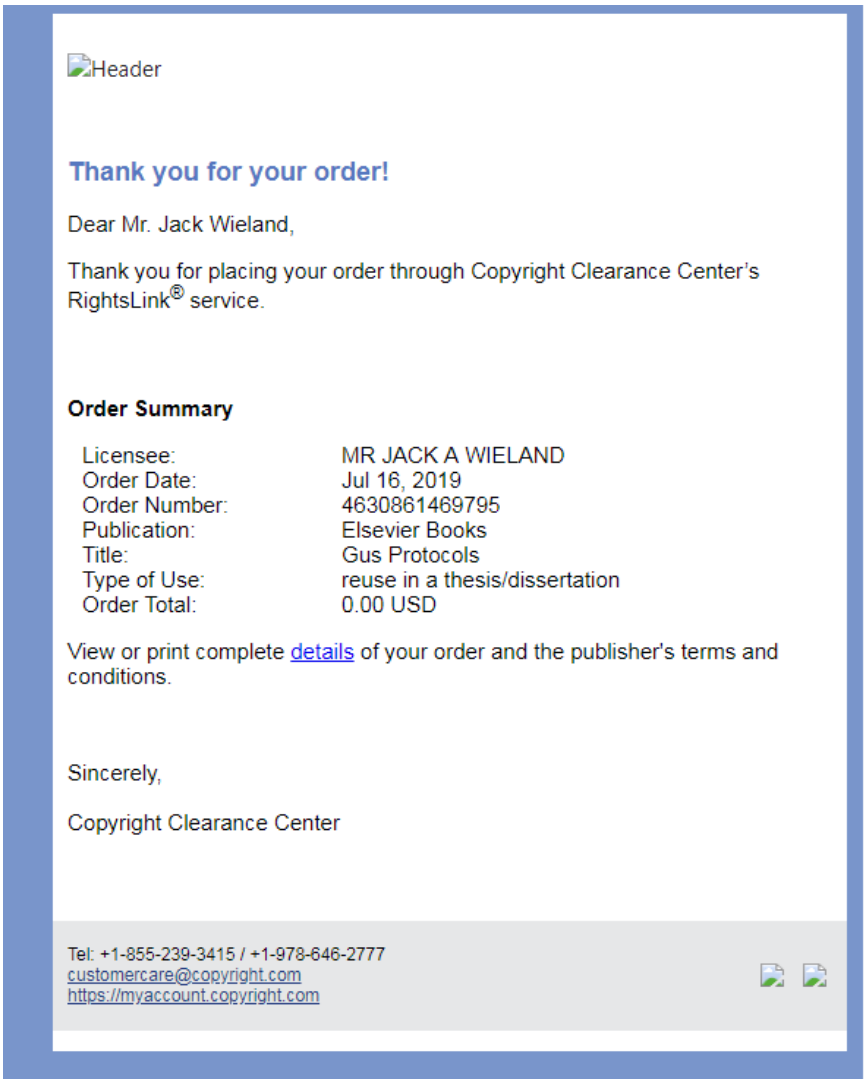

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Appendix 4: Supplementary information

A4 1.0: Organic anion transporters

Organic anion transporters (OATs) are 12 transmembrane (TMB) structures (Figure 4.2) which require sodium (Na^+) concentration gradients for molecule transportation. OATs are expressed in the kidneys and liver, on the basolateral surface of the membrane (Masuda et al. 1997; Takeuchi et al. 2001; Shikano et al. 2004; Eraly et al. 2006; Eraly et al. 2008; Zhu et al. 2012; Preising et al. 2015; Wu et al. 2017). OATs may work in conjunction with ABC transporters in a synergistic manner for molecule transportation. Alternatively, OATs may function independently without synergistic function with ABC transporters. An example of a predicted structure of a human OAT, OAT4, has been depicted in Figure A4 1.0

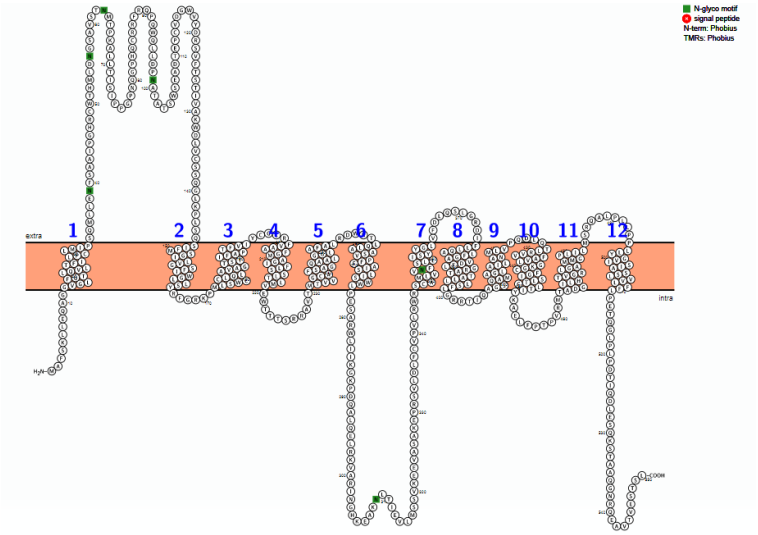


Figure A4 1.0: Predicted transmembrane topological structure of human organic anion transporter 4. Structure constructed using Protter (Omasits et al. 2014). OAT4 accession number: AAK68155.1

A5 1.2 Organic anion transporter regulation

OATs are subjected to regulation by PKC and ubiquitination. OAT1 for instance, is subjected ubiquitination degradation, with ten potential ubiquitination sites located between TMD2, 3, 6, 7, 8, 9 and on the C terminal (Li et al. 2013; Xu et

al. 2016). Degradation of OAT1 could lead to the development of certain diseases and conditions. For example, bilirubin is a substrate of OAT1, therefore OAT1 degradation could contribute to the development of jaundice.

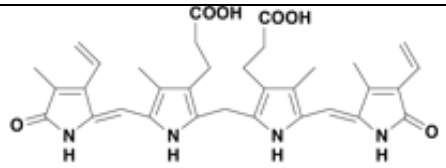
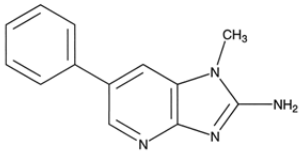
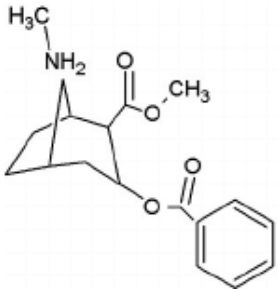
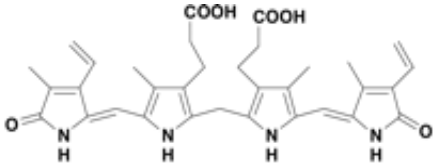
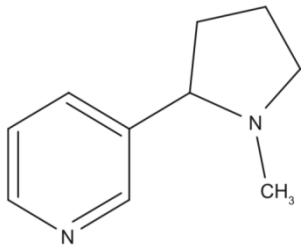
Table 1: Phosphorylation sites of ABC transporters PhosphoSitePlus®: Hombeck et al. (2004), was used to confirm the phosphorylation sites of ABC transporters.

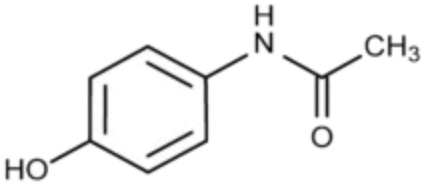
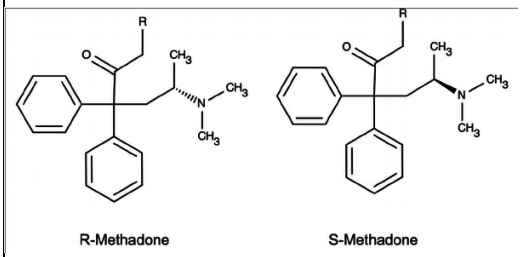
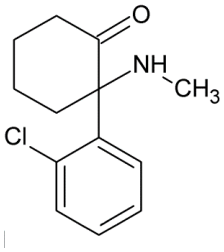
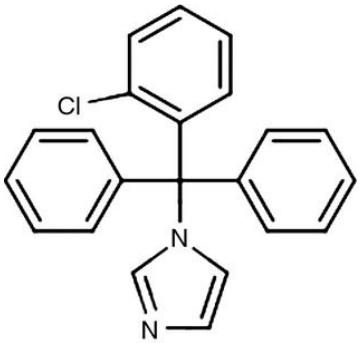
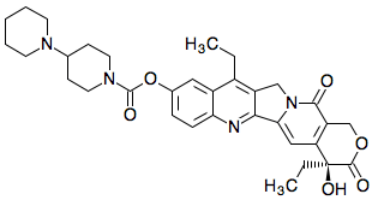
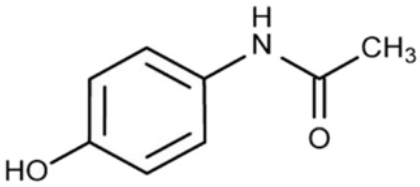
ABC Transporter	Amino acid residue	Amino acid position	Reference
ABCA1	Serine	1042	(Roosbeek et al. 2002)
	Threonine	1242	
	Threonine	1243	
	Serine	1255	
	Serine	2054	
ABCA2	Serine	1327	(Oslen et al. 2006)
	Serine	1331	
	Tyrosine	1694	(Rikova et al. 2007)
	Tyrosine	2178	(Dephoure et al. 2008)
	Tyrosine	2186	(Rikova et al. 2007)
	Threonine	2412	(Dephoure et al. 2008)
ABCA3	Tyrosine	1265	(Rikova et al. 2007; Cascado et al. 2013)
	Tyrosine	1268	
	Tyrosine	1349	
ABCA4	Tyrosine	901	(Tsybovsky et al. 2011)
ABCA5	Tyrosine	22	(Rikova et al. 2007
	Tyrosine	58	(Rikova et al. 2007
	Tyrosine	1299	(Hornbeck et al. 2004)
ABCA6	Tyrosine	464	(Gu et al. 2011)
	Serine	809	(Bian et al. 2014)
ABCA7	Serine	2133	(Bian et al. 2014)
ABCA8	Threonine	256	(Olsen et al. 2010)
	Serine	1507	(Olsen et al. 2010)
	Serine	1570	(Bian et al. 2014)
ABCA9	Serine	1333	(Mertins et al. 2014)
ABCA11	Serine	91	(Raijmakers et al. 2010)
	Threonine	112	(Yu et al. 2007)
	Threonine	115	
	Threonine	118	
ABCA13	Serine	2300	(Mertins et al. 2016)
	Tyrosine	3866	(Palacios-Moreno et al. 2015)

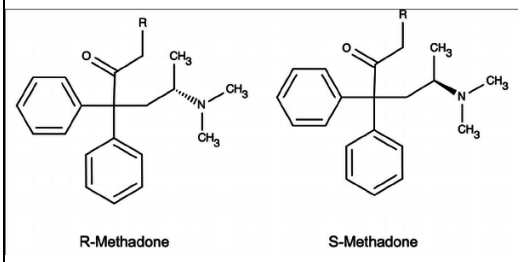
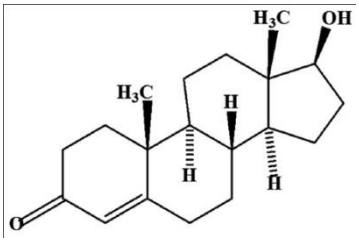
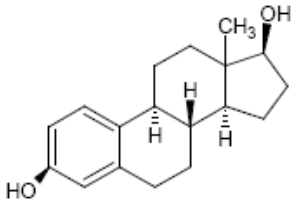
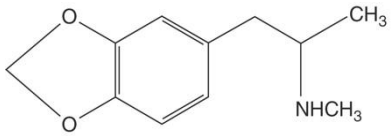
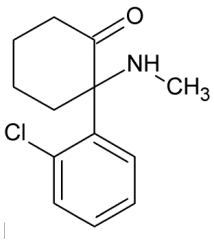
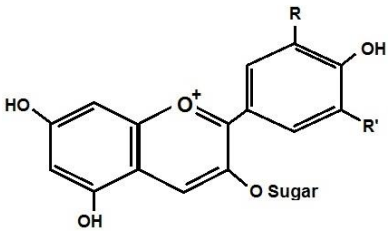
ABCB1	Serine	661	(Dephoure et al. 2008)
	Serine	667	(Chambers et al. 1994)
	Serine	683	
ABCB2	Threonine	545	(Mertins et al. 2016)
	Threonine	694	(Tsai et al. 2015)
ABCB3	Threonine	458	(Mertins et al. 2016)
ABCB4	**Not applicable**		
ABCB5	Threonine	1236	(Mertins et al. 2014)
ABCB6	Serine	456	(Stuart et al. 2015)
ABCB7	Serine	199	(Gu et al. 2011)
	Threonine	257	(Mertins et al. 2014)
	Threonine	600	(Tsai et al. 2015)
	Serine	743	(Mertins et al. 2016)
ABCB8	Serine	233	(Bian et al. 2014)
	Serine	544	(Mertins et al. 2014; Mertins et al. 2016)
	Serine	577	(Tsai et al. 2015)
ABCB9	**Not applicable**		
ABCB10	Threonine	363	(Alcolea et al. 2012)
ABCB11	Serine	690	(Bian et al. 2014)
	Serine	694	
	Serine	704	
ABCC1	Serine	915	(Palacios-Moreno et al. 2015)
	Serine	918	(Palacios-Moreno et al. 2015)
	Serine	930	(Mertins et al. 2016)
ABCC2	Serine	878	(Bian et al. 2014)
	Serine	930	Mertins et al. 2014
	Serine	938	(Bian et al. 2014)
	Serine	1153	(Zhao et al. 2011)
	Serine	1438	(Bian et al. 2014)
ABCC4	Serine	629	(Mertins et al. 2016)
	Threonine	646	(Mertins et al. 2016)
	Serine	655	(Mertins et al. 2016)
	Serine	668	(Mertins et al. 2016)
	Tyrosine	1259	(Tsai et al. 2015)

ABCC5	Serine	509	(Mertins et al. 2016)
	Serine	558	(Stuart et al. 2015)
	Tyrosine	1166	(Mortiz et al. 2010)
	Tyrosine	1423	(Palacios-Moreno et al. 2015)
ABCC6	Serine	294	(Klammer et al. 2012)
	Serine	681	(Gauci et al. 2009)
	Serine	902	(Yu et al. 2007)
	Serine	1286	(Bian et al. 2014)
	Serine	1310	(Gauci et al. 2009)
ABCC8	**Not applicable**		
ABCC9	Threonine	170	(Mertins et al. 2014)
ABCC10	Threonine	463	(Cantin et al. 2008)
	Serine	467	(Cantin et al. 2008)
ABCD4	Threonine	116	(Mertins et al. 2016)

Table 2: Structural comparison of phase I cytochrome p450 substrates in relation to the associated cytochrome p450.

Cytochrome p450 isoform	Molecule structure	Molecule name	Reference
CYP1A1		Bilirubin	(Zhang et al. 2005)
		PhIP	(Dingley et al. 1999)
		Cocaine	(Sanchez-Ramos 2004)
CYP1A2		Bilirubin	(Zhang et al. 2005)
		Nicotine	(Escobar-Chávez et al. 2011)

		Acetaminophen	(Singh et al. 2018)
CYP2B6		Methadone (R- and S-enantiomers)	(Bouquié et al. 2015)
		Ketamine	(Casale et al. 2012)
		Clotrimazole	(Crowley and Gallagher 2014)
CYP3A4		Irinotecan	(KEGG 2018)
		Acetaminophen	(Singh et al. 2018)

		Methadone (R- and S-enantiomers)	(Bouquié et al. 2015)
		Testosterone	(Almaiman 2018)
		Oestrogen (oestradiol)	(Revathi and Prashanth 2015)
		MDMA	(Hall and Henry 2006)
		Ketamine	(Casale et al. 2012)
		Anthocyanin	(Adedokun et al. 2016)

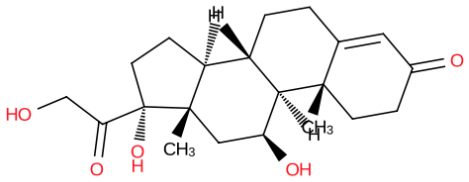
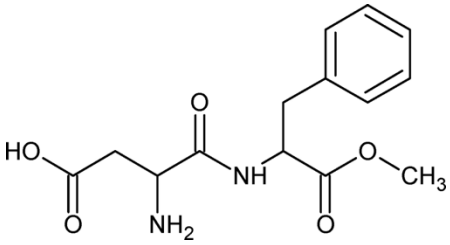
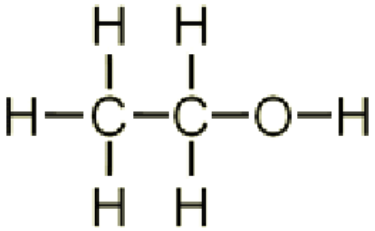
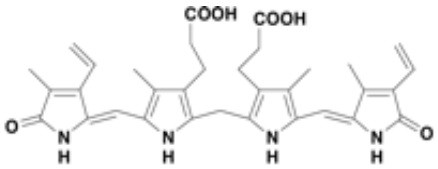
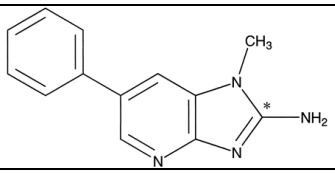
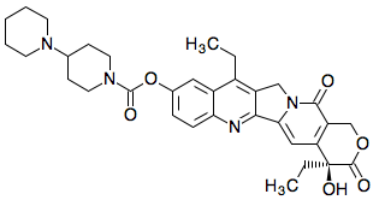
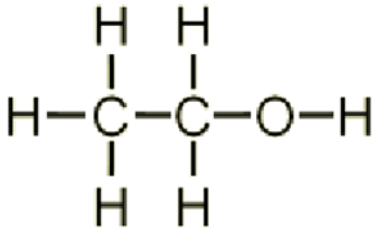
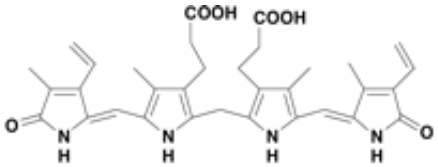
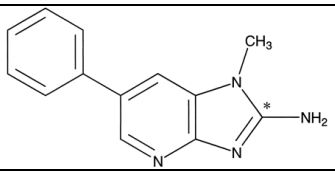
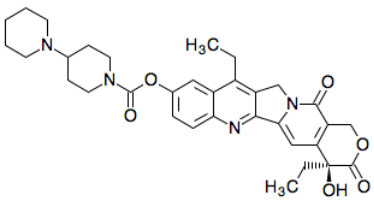
		Hydrocortisone	(EMBL-EBI 2019)
CYP2E1		Aspartame	(Magnuson et al. 2007)
		Ethanol	(Zaki et al. 2011)

Table 3: Phase II conjugation enzymes and associated substrate.

Phase II conjugation enzyme	Molecule structure	Molecule name	Reference for molecule structure
UGT1A1		Bilirubin	(Zhang et al. 2005)
		PhIP	(Dingley et al. 1999)
		Irinotecan	(KEGG 2018)
		Ethanol	(Zaki et al. 2011)
UGT1A6		Bilirubin	(Zhang et al. 2005)
		PhIP	(Dingley et al. 1999)
		Irinotecan	(KEGG 2018)

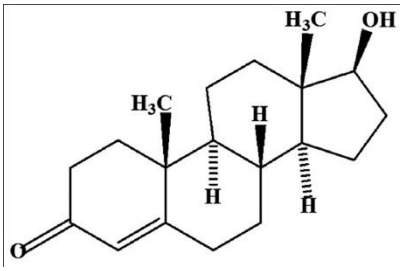
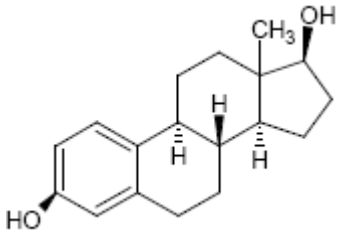
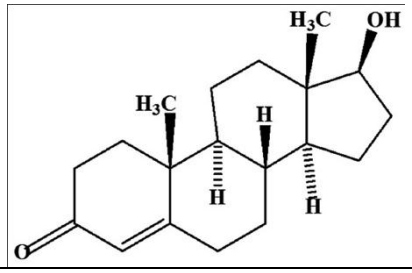
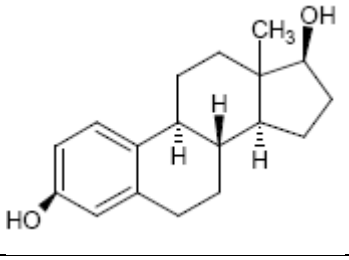
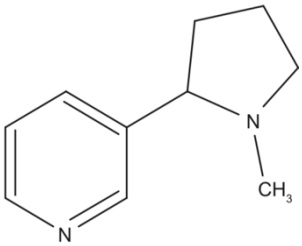
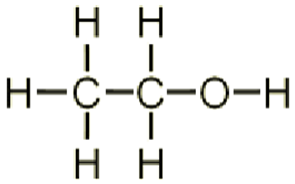
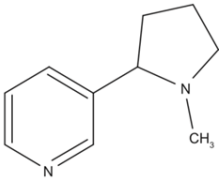
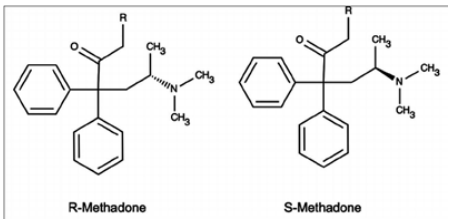
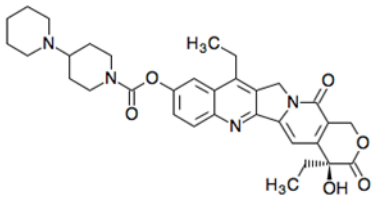
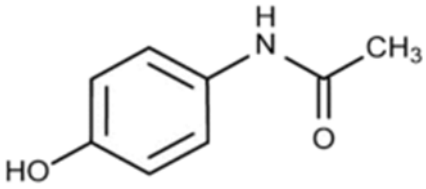
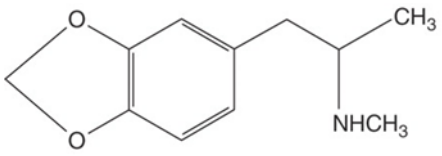
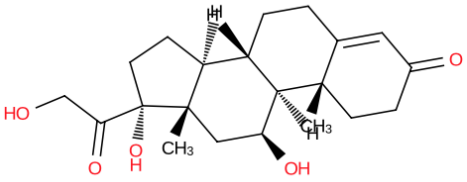
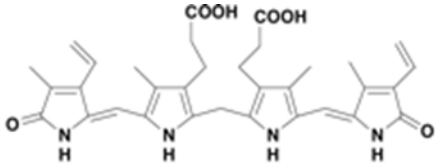
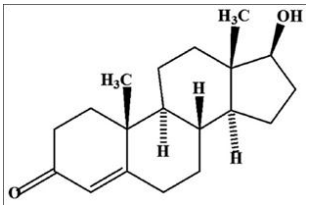
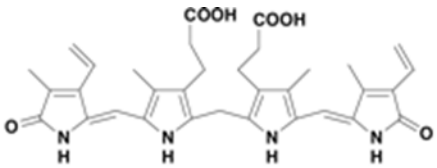
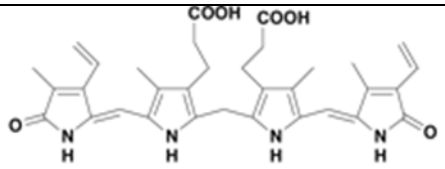
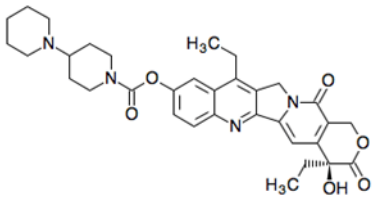
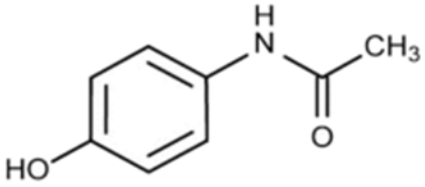
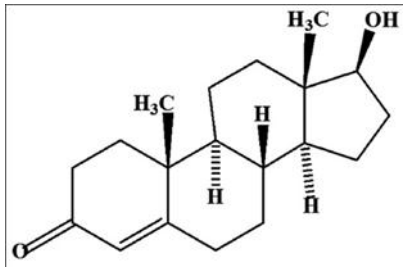
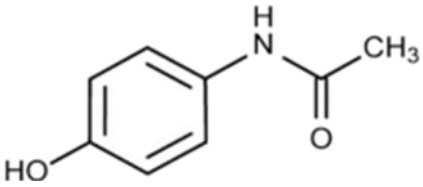
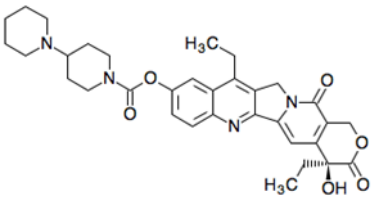
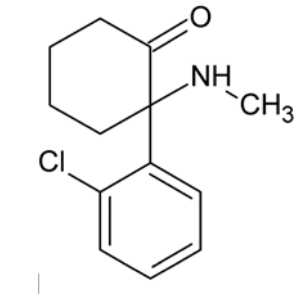
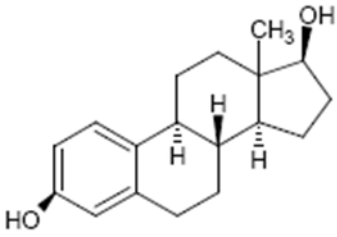
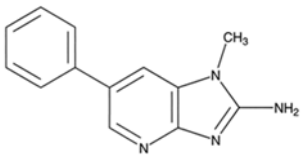
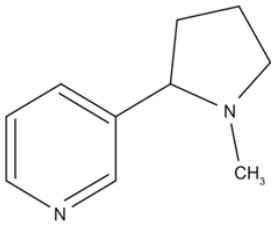
UGT2B15		Testosterone	(Almaiman 2018)
		Oestrogen (oestradiol)	(Revathi and Prashanth 2015)
UGT2B17		Testosterone	(Almaiman 2018)
		Oestrogen (oestradiol)	(Revathi and Prashanth 2015)
		Nicotine	(Escobar-Chávez et al. 2011)

Table 4: Phase III ABC transporters and molecule substrates

Phase III ABC transporter	Molecule structure	Molecule name	Reference for molecule structure
ABCA1 (Cholesterol Efflux Regulatory Protein)		Ethanol	(Zaki et al. 2011)
		Nicotine	(Escobar-Chávez et al. 2011)
ABCB1 (MDR1)		Methadone (R- and S-enantiomers)	(Bouquié et al. 2015)
		Irinotecan	(KEGG 2018)
		Acetaminophen	(Singh et al. 2018)

		MDMA	(Hall and Henry 2006)
		Hydrocortisone	(EMBL-EBI 2019)
ABCC1 (MRP1)		Bilirubin	(Zhang et al. 2005)
		Testosterone	(Almaiman 2018)
ABCC2 (MRP2)		Bilirubin	(Zhang et al. 2005)

ABCC3 (MRP3)		Bilirubin	(Zhang et al. 2005)
ABCC4 (MRR4)		Irinotecan	(KEGG 2018)
		Acetaminophen	(Singh et al. 2018)
		Testosterone	(Almaiman 2018)
ABCC12 (CFTR/MRP9)		Acetaminophen	(Singh et al. 2018)
ABCG2 (BCRP)		Irinotecan	(KEGG 2018)

		Ketamine	(Casale et al. 2012)
		Oestrogen (oestradiol)	(Revathi and Prashanth 2015)
		PhIP	(Dingley et al. 1999)
		Nicotine	(Escobar-Chávez et al. 2011)