

## What is Pharmacogenetics?

Pharmacogenetics seeks to understand how genes affect a person's response to drugs. This area of study is based on the understanding that drugs are eliminated through the biochemical pathways in a person's body, the compositions of which are determined by genes that synthesize proteins, including the enzymes that break down our bodies' chemicals and toxins.

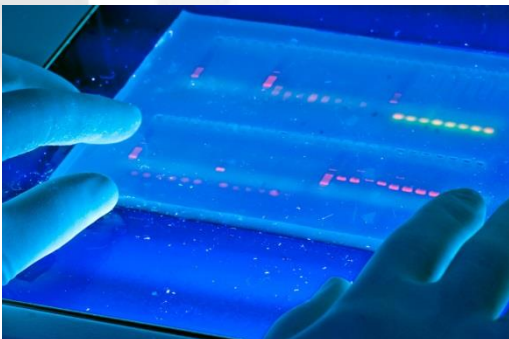


DNA analysis can be used to determine an individual's genetic and protein makeup. Knowing which genes a person has (or does not have) can indicate whether specific enzymes that depend on that pathway are impaired and therefore break down drugs more slowly or not at all. In some cases, enzymes can be "induced" meaning they break down drugs faster than normal. Overall drug response can be predicted by studying genes that influence any stage of the drug action pathway, including absorption, distribution, metabolism, and elimination.

Pharmacogenetics is distinct from pharmacogenomics which investigates how the whole genome (all the genes together) affects drug elimination, while pharmacogenetics focuses on individual genes. Both pharmacogenetics and pharmacogenomics comprise one aspect of a recent approach to medicine known as "personalized medicine" or "precision medicine". This is because studies on pharmacogenetics and pharmacogenomics seek to tailor health care to individual needs, and move away from a one-size-fits-all model of care.

## How is this information useful for clinicians?

Genetic testing can be used to predict an individual's response to different medications. This information may help determine which drugs and doses are appropriate for different people, and this can lead to improved drug effectiveness and reduced adverse reactions (including those from drug interactions). Successfully integrating genetic testing into clinical practice has the potential to help lower treatment costs by reducing hospital stays caused by adverse drug reactions or unresponsiveness to drugs that are a byproduct of the current "trial and error" treatment model.



Pharmacogenetic analysis has already proven useful with several drugs, including the following types:

- cardiovascular
- gastrointestinal
- breast cancer
- psychotropic

Antipsychotic medications can produce vastly different responses among individuals, so tailored prescribing could help make antipsychotic medication response more predictable and manageable. In addition, several large repositories of genetic data have been created in recent years that can be used to help clinical interpretation. It is possible that in the future, people's genetic data will be integrated with their electronic medical record (EMR).

Pharmacogenetics has the potential to refine treatment of drug addiction, which is based on a complex interaction of biological, environmental, psychological, and drug use factors. Incorporating pharmacogenetics into drug development can also be used to reduce harmful side effects of drugs, such as weight gain from antipsychotics. Studies have shown that health care providers are generally optimistic about the utility of pharmacogenetic testing in a clinical setting.

While not routinely available, Dr. Aitchison, based at the University of Alberta, has conducted genetic testing for antidepressant and antipsychotic drug response and is currently working on making this available in Alberta. Patients may ask their physicians if they feel it might be beneficial to them, and physicians may contact Dr. Aitchison directly.

### **What research has been conducted on pharmacogenetics by the current Alberta Centennial Addiction and Mental Health Research Chair?**

Dr. Aitchison has conducted research in the following areas of pharmacogenetic research:

- How genetics can inform management of cognitive deficits in schizophrenia
- Cytochrome P450 2C19 (CYP2C19) genotype and escitalopram concentration in the treatment of depression
- Changes in gene expression in response to antidepressants in the developing brain
- How genotypes of two enzymes confer increased risk of potentially lethal low sodium when taking the drug "Ecstasy"
- How genotypes of the same enzymes confer increased risk of potentially neurotoxic levels of the hormone cortisol when taking the drug "Ecstasy"
- Genetic predisposition to the development of the potentially permanent neurological movement disorder tardive dyskinesia as a side effect of antipsychotics
- Association of a genetic marker with memory difficulties in individuals vulnerable to psychotic illness
- Genes that predispose to the development of schizophrenia and associated neuroimaging changes in the brain

Learn more about Dr. Aitchison's research at:

- [The Alberta Addiction and Mental Health Research Partnership Program](#)
- [The University of Alberta Department of Psychiatry](#)

## Where can I find more information on pharmacogenetics?

The [Canadian Institutes of Health Research](#) provide [information about Personalized Medicine](#), one of their signature initiatives.

The [Centre for Addiction and Mental Health](#) has a [pharmacogenetics program](#) that is dedicated to understanding how patients' genetic profiles affect their responses to psychiatric medication.

Annual [Pharmacogenetics in Psychiatry Meetings](#) provide a forum for presenting and discussing new developments in the rapidly developing field of psychiatric pharmacogenetics.

The [Centre for Mental Health Initiatives](#) at the [Johns Hopkins Bloomberg School of Public Health](#) is establishing a database of psychiatric treatment information, including patient history and medication response. A range of genome-wide association studies with targeted pharmacogenetic outcomes will be conducted on the data.

The [Addiction Genetics and Pharmacogenetics Division](#) at the [University of Pennsylvania Perelman School of Medicine](#) focuses on how genetic variation and epigenetics act as risk factors to addiction, and affect the outcomes of psychosocial and pharmacological treatments.

The [Canadian Pharmacogenomics Network for Drug Safety](#) is based out of the University of British Columbia and focuses on finding drug safety solutions to combat adverse drug reactions.

The [Canadian Society of Pharmacology and Therapeutics](#) provides [clinical practice guidelines](#) for pharmacogenetic testing.

The [Pharmacogenetics Knowledgebase](#) provides information to researchers about genetic variations, annotations, drug pathways and their relationships with drug response. The [Clinical Pharmacogenetics Implementation Consortium](#) (through the same organization) provides clinical practice and drug dosing guidelines, as well as information on drug and food interactions, and metabolic enzymes.

## References

- Aitchison, K. J.**, & Reynolds, G. P. (2012). Special issue on Pharmacogenetics. *Journal of Psychopharmacology*, 26(3), 333. <http://doi.org/10.1177/0269881112439150>
- Aitchison, K. J.**, Tsapakis, E. M., Huezo-Diaz, P., Kerwin, R. W., Forsling, M. L., & Wolff, K. (2012). Ecstasy (MDMA)-induced hyponatraemia is associated with genetic variants in CYP2D6 and COMT. *Journal of Psychopharmacology*, 26(3), 408–418. <http://doi.org/10.1177/02698811111434624>
- Avoiding weight gain from antipsychotic medications. (2015). *CAMH Discovers, Fall 2015*. Retrieved from [http://www.camh.ca/en/research/news\\_and\\_publications/CAMH-Discovers/fall-2015/Pages/Avoiding-weight-gain-from-antipsychotic-medications.aspx](http://www.camh.ca/en/research/news_and_publications/CAMH-Discovers/fall-2015/Pages/Avoiding-weight-gain-from-antipsychotic-medications.aspx)
- Bernier, D., Macintyre, G., Bartha, R., Hanstock, C. C., McAllindon, D., Cox, D., Purdon, S., **Aitchison, K. J.**, Rusak, B., & Tibbo, P. G. (2014). NPAS3 variants in schizophrenia: a neuroimaging study. *BMC Medical Genetics*, 15(37). <http://doi.org/10.1186/1471-2350-15-37>
- Carvalho Henriques, B., Heywood, B. A., Malhotra, A. K., & **Aitchison, K. J.** (2014). *PIP 2014—Pharmacogenetics in psychiatry*. Report on the 13th Annual Pharmacogenetics in Psychiatry Meeting, Hollywood, FL. Retrieved from <http://www.schizophreniaforum.org/new/detail.asp?id=2129>
- Colizzi, M., Iyegbe, C., Powell, J., Ursini, G., Porcelli, A., Bonvino, A., Taurisano, P., Romano, R., Masellis, R., Blasi, G., Morgan, C., **Aitchison, K.**, Mondelli, V., Luzi, S., Kolliakou, A., David, A., Murray, R. M., Bertolino, A., & Di Forti, M. (2015). Interaction between functional genetic variation of DRD2 and cannabis use on risk of psychosis. *Schizophrenia Bulletin*, 41(5), 1171–1182. <http://doi.org/10.1093/schbul/sbv032>
- Dorfman, E. H., Brown Trinidad, S., Morales, C. T., Howlett, K., Burke, W., & Woodahl, E. L. (2015). Pharmacogenomics in diverse practice settings: implementation beyond major metropolitan areas. *Pharmacogenomics*, 16(3), 227–237. <http://doi.org/10.2217/pgs.14.174>
- Durham, D. (2014). Utilizing pharmacogenetics in psychiatry: the time has come. *Molecular Diagnosis & Therapy*, 18(2), 117–119. <http://doi.org/10.1007/s40291-014-0085-4>
- Ho, M. K., Goldman, D., Heinz, A., Kaprio, J., Kreek, M. J., Li, M. D., Munafò, M. R., & Tyndale, R. F. (2010). Breaking barriers in the genomics and pharmacogenetics of drug addiction. *Clinical Pharmacology & Therapeutics*, 88(6), 779–791. <http://doi.org/10.1038/clpt.2010.175>
- Hodgson, K., Tansey, K. E., Powell, T. R., Coppola, G., Uher, R., Zvezdana Dernovšek, M., Mors, O., Hauser, J., Souery, D., Maier, W., Henigsberg, N., Rietschel, M., Placentino, A., **Aitchison, K. J.**, Craig, I. W., Farmer, A. E., Breen, G., McGuffin, P., & Dobson, R. (2015). Transcriptomics and the mechanisms of antidepressant efficacy. *European Neuropsychopharmacology*, 26(1), 105–112. <http://doi.org/10.1016/j.euroneuro.2015.10.009>
- Hodgson, K., Tansey, K., Dernovsek, M. Z., Hauser, J., Henigsberg, N., Maier, W., Mors, O., Placentino, A., Rietschel, M., Souery, D., Smith, R., Craig, I. W., Farmer, A. E., **Aitchison, K. J.**, Belsy, S., Davis, O. S. P., Uher, R., & McGuffin, P. (2014). Genetic predictors of antidepressant side effects: a grouped candidate gene approach in the Genome-Based Therapeutic Drugs for Depression (GENDEP) study. *Journal of Psychopharmacology*, 28(2), 142–150. <http://doi.org/10.1177/0269881113517957>
- Huezo-Diaz, P., Perroud, N., Spencer, E. P., Smith, R., Sim, S., Viriding, S., Uher, R., Gunasinghe, C., Gray, J., Campbell, D., Hauser, J., Maier, W., Marusic, A., Rietschel, M., Perez, J., Giovannini, C., Mors, O., Mendlewicz, J., McGuffin, P., Farmer, A. E., Ingelman-Sundberg, M., Craig, I. W., & **Aitchison, K. J.**

- (2012). CYP2C19 genotype predicts steady state escitalopram concentration in GENDEP. *Journal of Psychopharmacology*, 26(3), 398–407. <http://doi.org/10.1177/0269881111414451>
- Jakka, S., & Rossbach, M. (2013). An economic perspective on personalized medicine. *The HUGO Journal*, 7(1), 1. <http://doi.org/10.1186/1877-6566-7-1>
- Jones, J. D., Comer, S. D., & Kranzler, H. R. (2015). The pharmacogenetics of alcohol use disorder. *Alcoholism, Clinical and Experimental Research*, 39(3), 391–402. <http://doi.org/10.1111/acer.12643>
- Khalsa, S. (2015). Pharmacogenetics: what it is and why you need to know. Retrieved December 16, 2015, from [http://www.huffingtonpost.com/dr-soram-khalsa/pharmacogenetics-what-it-is\\_b\\_7683164.html](http://www.huffingtonpost.com/dr-soram-khalsa/pharmacogenetics-what-it-is_b_7683164.html)
- Koola, M. M., Buchanan, R. W., Pillai, A., **Aitchison, K. J.**, Weinberger, D. R., Aaronson, S. T., & Dickerson, F. B. (2014). Potential role of the combination of galantamine and memantine to improve cognition in schizophrenia. [Review]. *Schizophrenia Research*, 157(1-3), 84–89. <http://doi.org/10.1016/j.schres.2014.04.037>
- Koola, M. M., Tsapakis, E. M., Wright, P., Smith, S., Kerwin, R. W., Nugent, K. L., & **Aitchison, K. J.** (2014). Association of tardive dyskinesia with variation in CYP2D6: Is there a role for active metabolites? *Journal of Psychopharmacology*, 28(7), 665–670. <http://doi.org/10.1177/0269881114523861>
- Lodhi, R., Rossolatos, D., & **Aitchison, K. J.** (in press). Genetics and genomics in addiction research. In K. Wolff, J. White, & S. Karch (Eds.), *The SAGE Handbook of Drug & Alcohol Studies Volume 2: Biological Approaches*. New York, NY: SAGE Publications.
- Olson, S., Beachy, S. H., Giammaria, C. F., Berger, A. C., Roundtable on translating genomic-based research for health, Board on Health Sciences Policy, & Institute of Medicine. (2012). *Integrating Large-Scale Genomic Information into Clinical Practice: Workshop Summary*. Washington, DC: National Academies Press. Retrieved from <http://www.nap.edu/catalog/13256>
- Pouget, J. G., Shams, T. A., Tiwari, A. K., & Müller, D. J. (2014). Pharmacogenetics and outcome with antipsychotic drugs. *Dialogues in Clinical Neuroscience*, 16(4), 555–566.
- Relling, M. V., & Evans, W. E. (2015). Pharmacogenomics in the clinic. *Nature*, 526(7573), 343–350. <http://doi.org/10.1038/nature15817>
- Rens, N. (2013, August 3). *What is Genomics?* [Video file]. Retrieved from <https://www.youtube.com/watch?v=BoUS6mxnIE>
- Rossolatos, D., & **Aitchison, K. J.** (2014). Genomics for clinical utility: the future is near. *Genome Medicine*, 6(1). <http://doi.org/10.1186/gm522>
- Tansey, K. E., Rucker, J. J. H., Kavanagh, D. H., Guipponi, M., Perroud, N., Bondolfi, G., Domenici, E., Evans, D. M., Hauser, J., Henigsberg, N., Jerman, B., Maier, W., Mors, O., O'Donovan, M., Peters, T. J., Placentino, A., Rietschel, M., Souery, D., **Aitchison, K. J.**, Craig, I., Farmer, A., Wendland, J. R., Malafosse, A., Lewis, G., Kapur, S., McGuffin, P., & Uher, R. (2014). Copy number variants and therapeutic response to antidepressant medication in major depressive disorder. *Pharmacogenomics Journal*, 14(4), 395–399. <http://doi.org/10.1038/tpj.2013.51>
- Thompson, C., Hamilton, S. P., & Hippman, C. (2015). Psychiatrist attitudes towards pharmacogenetic testing, direct-to-consumer genetic testing, and integrating genetic counseling into psychiatric patient care. *Psychiatry Research*, 226(1), 68–72. <http://doi.org/10.1016/j.psychres.2014.11.044>

- Tsapakis, E. M., Curran, S., Ohlsen, R. I., Vyas, N. S., **Aitchison, K. J.**, & Daly, A. K. (2012). Pharmacogenetics in Psychiatry. In A.-H. Maitland-van der Zee & A. K. Daly (Eds.), *Pharmacogenetics and Individualized Therapy* (pp. 215–250). Hoboken, NJ: Wiley.
- Tsapakis, E. M., Fernandes, C., Moran-Gates, T., Basu, A., Sugden, K., **Aitchison, K. J.**, & Tarazi, F. I. (2014). Effects of antidepressant drug exposure on gene expression in the developing cerebral cortex. *Synapse*, 68(5), 209–220. <http://doi.org/10.1002/syn.21732>
- Vyas, N. S., Ahn, K., Stahl, D. R., Caviston, P., Simic, M., Netherwood, S., Puri, B. K., Lee, Y., & **Aitchison, K. J.** (2014). Association of KIBRA rs17070145 polymorphism with episodic memory in the early stages of a human neurodevelopmental disorder. *Psychiatry Research*, 220(1-2), 37–43. <http://doi.org/10.1016/j.psychres.2014.07.024>
- Vyas, N. S., Shamsi, S. A., Malhotra, A. K., **Aitchison, K. J.**, & Kumari, V. (2012). Can genetics inform the management of cognitive deficits in schizophrenia? *Journal of Psychopharmacology*, 26(3), 334–348. <http://doi.org/10.1177/02698811111434623>
- Wen, J.-G., Wu, L., Pu, X.-X., He, F.-Z., Liu, M.-Z., Zhou, H.-H., & Zhang, W. (2015). Pharmacogenomics research: a potential strategy for drug development. *Die Pharmazie*, 70(7), 437–445.
- Wolff, K., Tsapakis, E. M., Pariante, C. M., Kerwin, R. W., Forsling, M. L., & **Aitchison, K. J.** (2012). Pharmacogenetic studies of change in cortisol on ecstasy (MDMA) consumption. *Journal of Psychopharmacology*, 26(3), 419–428. <http://doi.org/10.1177/02698811111415737>
- Zhang, G., Zhang, Y., Ling, Y., & Jia, J. (2015). Web resources for pharmacogenomics. *Genomics, Proteomics & Bioinformatics*, 13(1), 51–54. <http://doi.org/10.1016/j.gpb.2015.01.002>
- Zhang, J.-P., **Aitchison, K. J.**, & Malhotra, A. K. (2014). The 12th Annual Pharmacogenetics in Psychiatry meeting report. *Psychiatric Genetics*, 24(5), 218–220. <http://doi.org/10.1097/YPG.0000000000000041>

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