Title

Evaluation of linkage disequilibrium between CYP2D6 gene polymorphisms associated with breast cancer in women; [Evaluación del desequilibrio de ligamiento entre los polimorfismos del gen CYP2D6 asociados a cáncer de mama en mujeres]

Abstract

Introduction: the CYP2D6 gene is highly polymorphic and is involved in the metabolism of a wide variety of drugs and xenobiotics. Three allelic variants of the gene (rs3892097, rs1065852 and rs28371725) have been studied in relation to breast cancer, but the degree of genetic linkage between them is unknown. Objetive: to test whether the three breast cancer-associated SNPs are inherited en bloc. Methods: genotypes of 280 SNPs of the CYP2D6 gene were obtained from the 1000Genomes database and linkage disequilibrium between the three breast cancer-associated SNPs and the other 277 SNPs in the gene was analysed. A threshold of r2= 0,7 was used to identify loci in linkage disequilibrium. Results: a strong correlation was found between rs3892097 and rs1065852 in Europe and Latin America. In addition, eleven polymorphisms with a high level of linkage were identified, four of which have a non-synonymous mutation effect. Conclusions: both polymorphisms could have a causal effect on breast cancer or that one of them is associated by linkage. Continuing to study both polymorphisms and considering the eleven new polymorphisms for analysis would be of relevance to deepen knowledge in relation to breast cancer in women.

Authors

Flores S.V.; Roco-Videla A.; Aguilera-Eguía R.; Montaña R.

Author full names

Flores, Sergio Vladimir (57536122800); Roco-Videla, Angel (57197820869); Aguilera-Eguía, Raúl (30867480100); Montaña, Román (58866308300)

Author(s) ID

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Affiliations

Universidad Arturo Prat, Iquique, Chile; Universidad Bernardo O'Higgins, Programa de Magister en Ciencias Químico-Biológicas, Santiago, Chile; Universidad Católica de la Santísima Concepción, Departamento de Salud Pública, Concepción, Chile; Universidad Autónoma de Chile, Facultad de Ciencias de la Salud, Santiago, Chile

Authors with affiliations

Flores S.V., Universidad Arturo Prat, Iquique, Chile; Roco-Videla A., Universidad Bernardo O'Higgins, Programa de Magister en Ciencias Químico-Biológicas, Santiago, Chile; Aguilera-Eguía R., Universidad Católica de la Santísima Concepción, Departamento de Salud Pública, Concepción, Chile; Montaña R., Universidad Autónoma de Chile, Facultad de Ciencias de la Salud, Santiago, Chile

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References

Avsar O., Identification of the effects of pathogenic genetic variations of human CYP2C9 and CYP2D6: an in silico approach, Nucleosides Nucleotides Nucleic Acids,

43, pp. 356-376, (2024); Hennig EE, Piatkowska M, Goryca K, Pospiech E, Paziewska A, Karczmarski J, Et al., Non-CYP2D6 variants selected by a GWAS improve the prediction of impaired tamoxifen metabolism in patients with breast cancer, J Clin Med, 8, (2019); Sanchez-Spitman AB, Bohringer S, Dezentje VO, Gelderblom H, Swen JJ, Guchelaar H-J., A genome-wide association study of endoxifen serum concentrations and adjuvant tamoxifen efficacy in early-stage breast cancer patients, Clin Pharmacol Ther, (2024); Smith D, He B, Shi J, Zhu H-J, Wang X., Novel independent trans-and Cis-genetic variants associated with CYP2D6 expression and activity in human livers, Drug Metab Dispos, 52, pp. 143-152, (2024); Khor CC, Winter S, Sutiman N, Murdter TE, Chen S, Lim JSL, Et al., Cross-ancestry genome-wide association study defines the extended CYP2D6 locus as the principal genetic determinant of endoxifen plasma concentrations, Clin Pharmacol Ther, 113, pp. 712-723, (2023); Goetz MP, Knox SK, Suman VJ, Rae JM, Safgren SL, Ames MM, Et al., The impact of cytochrome P450 2D6 metabolism in women receiving adjuvant tamoxifen, Breast Cancer Res Treat, 101, pp. 113-121, (2007); Stingl JC, Parmar S, Huber-Wechselberger A, Kainz A, Renner W, Seeringer A, Et al., Impact ofCYP2D6*4genotype on progression free survival in tamoxifen breast cancer treatment, Curr Med Res Opin, 26, pp. 2535-2542, (2010); Wegman P, Elingarami S, Carstensen J, Stal O, Nordenskjold B, Wingren S., Genetic variants of CYP3A5, CYP2D6, SULT1A1, UGT2B15 and tamoxifen response in postmenopausal patients with breast cancer, Breast Cancer Res, 9, (2007); Sukasem C, Chamnanphon M, Pechatanan K, Santon Puangpetch, Chantratita W, Et al., Association of CYP2D6 and CYP2C19 polymorphisms and disease-free survival of Thai post-menopausal breast cancer patients who received adjuvant tamoxifen, Pharmgenomics Pers Med, (2013); Lim JSL, Chen XA, Singh O, Yap YS, Ng RCH, Wong NS, Et al., Impact of CYP2D6, CYP3A5, CYP2C9 and CYP2C19 polymorphisms on tamoxifen pharmacokinetics in Asian breast cancer patients, Br J Clin Pharmacol, 71, pp. 737-750, (2011); Schroth W, Antoniadou L, Fritz P, Schwab M, Muerdter T, Zanger

UM, Et al., Breast cancer treatment outcome with adjuvant tamoxifen relative to patient CYP2D6 and CYP2C19 genotypes, J Clin Oncol, 25, pp. 5187-5193, (2007); Qanbari S., On the extent of linkage disequilibrium in the genome of farm animals, Front Genet, 10, (2020); Fairley S, Lowy-Gallego E, Perry E, Flicek P., The International Genome Sample Resource (IGSR) collection of open human genomic variation resources, Nucleic Acids Res, 48, pp. D941-D947, (2020); Byrska-Bishop M, Evani US, Zhao X, Basile AO, Abel HJ, Regier AA, Et al., High-coverage whole-genome sequencing of the expanded 1000 Genomes Project cohort including 602 trios, Cell, 185, pp. 3426-3440, (2022); Danecek P, Auton A, Abecasis G, Albers CA, Banks E, DePristo MA, Et al., The variant call format and VCFtools, Bioinformatics, 27, pp. 2156-2158, (2011); Boullerne AI, Goudey B, Paganini J, Erlichster M, Gaitonde S, Feinstein DL., Validation of tag SNPs for multiple sclerosis HLA risk alleles across the 1000 genomes panel, Hum Immunol, 2024; Wray NR., Allele frequencies and ther2measure of linkage disequilibrium: Impact on design and interpretation of association studies, Twin Res Hum Genet, 8, pp. 87-94, (2005); Habib I, Khan S, Mohammad T, Hussain A, Alajmi MF, Rehman T, Et al., Impact of non-synonymous mutations on the structure and function of telomeric repeat binding factor 1, J Biomol Struct Dyn, 40, pp. 9053-9066, (2022); Booker TR, Yeaman S, Whitlock MC., Variation in recombination rate affects detection of outliers in genome scans under neutrality, bioRxiv, (2020); Li R, Budowle B, Sun H, Ge J., Linkage and linkage disequilibrium among the markers in the forensic MPS panels, J Forensic Sci, 66, pp. 1637-1646, (2021); Pingault J-B, Rijsdijk F, Schoeler T, Choi SW, Selzam S, Krapohl E, Et al., Genetic sensitivity analysis: Adjusting for genetic confounding in epidemiological associations, PLoS Genet, 17, (2021)

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