



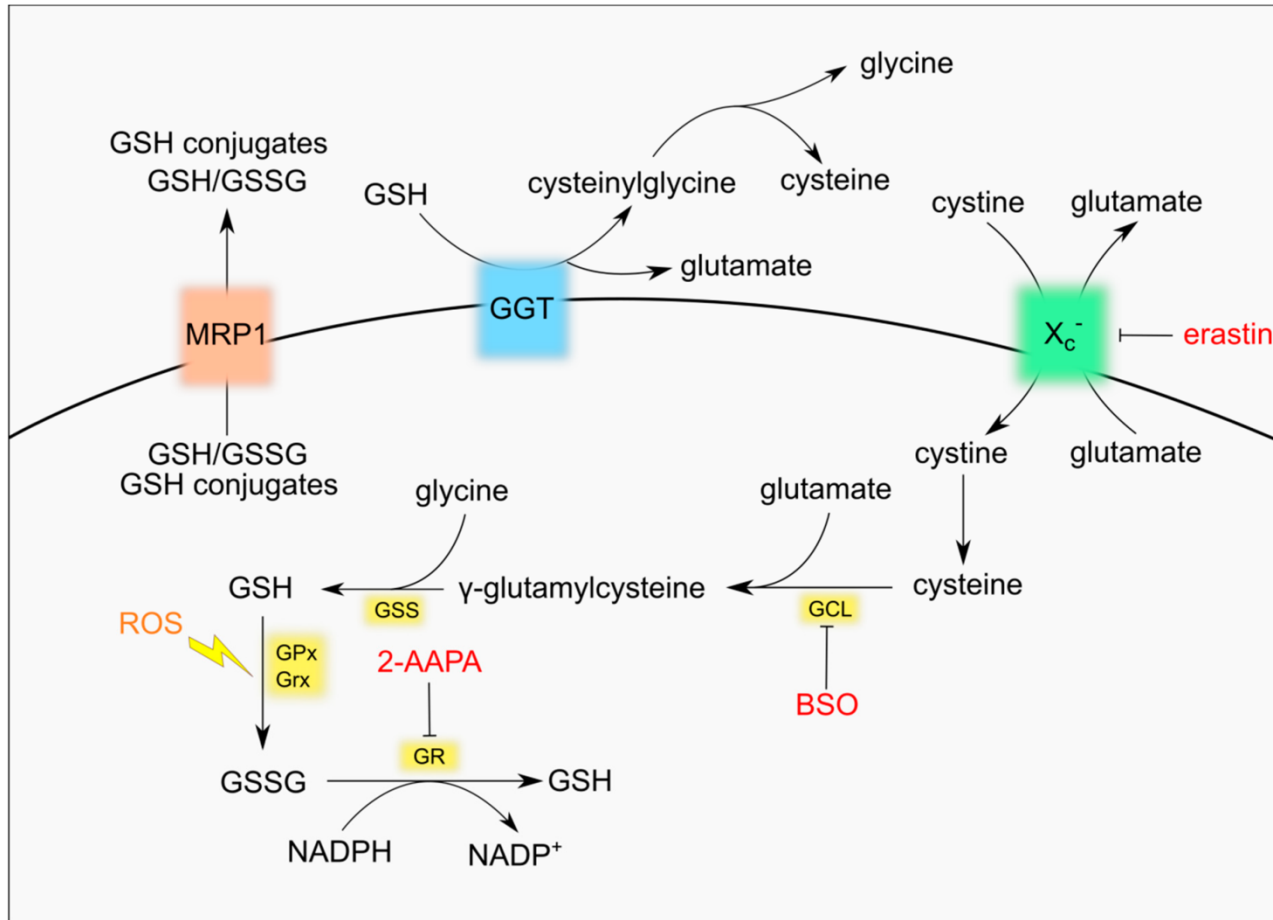
Polymorphism in genes involved in glutathione metabolism is associated with the risk of uterine fibroids

**Kudryavtseva O.^{1,2}, Kobzeva K.¹, Vdovina I.^{1,2}, Ponomareva L.¹,
Polonikov A.¹, Bushueva O.¹**

¹ Kursk State Medical University, Kursk, Russia

² Kursk Regional Clinical Hospital, Kursk, Russia

Glutathione metabolism



Desideri, E., Ciccarone, F., & Ciriolo, M. R. (2019). Targeting glutathione metabolism: partner in crime in anticancer therapy. *Nutrients*, 11(8), 1926.

Aim

The aim of our study was to analyze the role of polymorphic variants of genes involved in glutathione metabolism in the development of uterine fibroids .

Material and methods

Genotyping

N=889

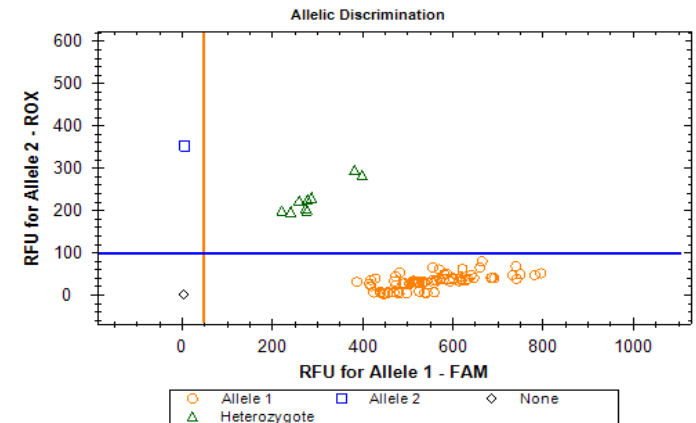
Uterine fibroids patients (N=552)

Controls (N=337)

Genotyping: 13 genetic variants:

rs713041 *GPX4*, rs4902346 *GPX2*, rs41303970 *GCLM*,
rs17883901 *GCLC*, rs1050450 *GPX1*, rs1799811, rs1695
GSTP1, rs2551715 *GSR*, rs1801310 *GSS*, rs4820599
GGT1, rs7674870 *SLC7A11* (TaqMan-based PCR; CFX96,
Bio-Rad).

+/- *GSTM1*, +/- *GSTT1* (multiplex PCR).



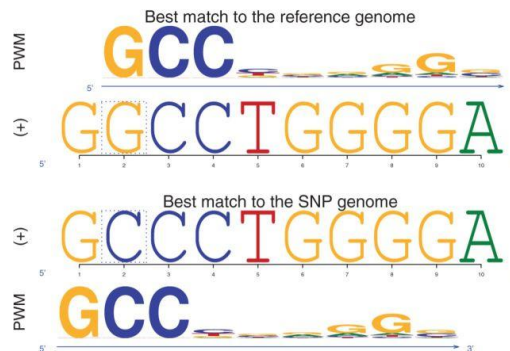
Statistical analysis: SNPStats (<https://www.snpstats.net/start.htm>) with adjustment for age.

Bioinformatics analysis

 GTEX Portal

"Viewing Gene Expression Data on the GTEX Portal"

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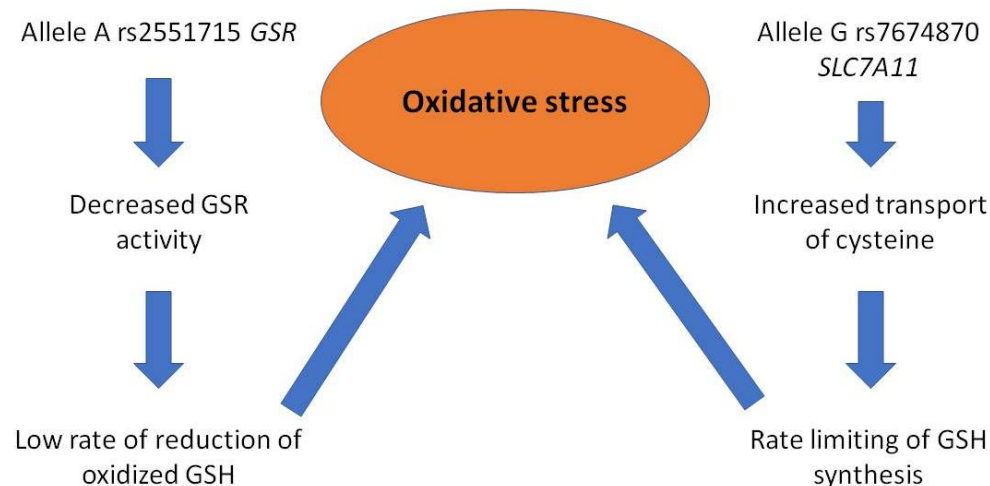



GENE ONTOLOGY

Statistically significant associations of SNPs in genes Glutathione metabolism with the risk of uterine fibroids

SNP	Results of analysis of associations
rs2551715 <i>GSR</i>	OR = 0.83, 95%CI = 0.70-0.99, P = 0.04
rs7674870 <i>SLC7A11</i>	OR= 1.25, 95%CI = 1.03-1.50, P = 0.02

Protective allele A rs7674870 *SLC7A11* \longrightarrow 16 transcription factors (TFAP2A, NFIC, SP2, PAX9, RUNX1, RUNX3, RUNX2, PAX1, TFAP2, TFAP2C, NFIB, TFAP2A, DMRTC2, RAD21, RUNX3, E2F4) \longrightarrow jointly involved in the regulation of cell population proliferation (GO:0042127; FDR = 6.57×10^{-3}).



Conclusion

Thus, we have carried out a comprehensive analysis of the involvement of glutathione metabolism genes in predisposition to uterine fibroids. An association of single nucleotide polymorphisms rs7674870 *SLC7A11* and rs2551715 *GSR* with the risk of uterine fibroids was found for the first time.