Cytochrome P450

Introduction

Cytochromes P450 (*'CYP'*) are enzymes of the cytochrome family, ie enzymes originally discovered as cellular [[pigment] pigments]] (hence the name <! - reference -> [& amp; amp; dagger; 1] <! - end of reference ->), which contain porphyrin with an iron atom as the central atom with coordination number 6 (unlike hemoglobin [& amp; dagger; 1]), which transitions between states Fe 2+ / Fe 3+ < / sup> performs electron transfer and thus **oxidation-reduction reactions**

(often monooxygenation). It is involved in both the metabolism of some endogenous metabolites and the biotransformation of most xenobiotics [1]. Human genome contains 57 cytochrome P450 genes [2], the organism expresses about 100 isoforms [1], mostly in the liver.

They catalyze the reaction

$$mathrmRH + mathrmO_2 + 2\,mathrmH^+ + 2e^- rightleftharpoons mathrmROH + mathrmH_2\,mathrmO$$

for which they use cytochrome P450 reductase-mediated cofactor NADPH as a source of electrons [1].

Families 1, 2 and 3 of cytochrome P450 are mainly involved in the metabolism of xenobiotics, while families 4-51 are mainly involved in the metabolism of endogenous substances such as sterols, steroids, bile acids and fatty acids [2].

Metabolism of xenobiotics

Polymorphism

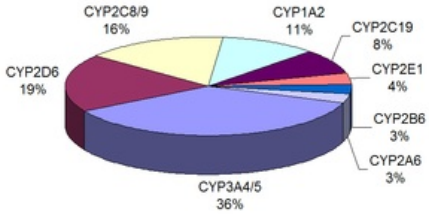
'Cytochromes P450' show an unusual polymorphism. Several situations can occur in a population for a given gene encoding enzyme of the cytochrome P450 family [2]:

- alleles carry copies of the gene, so there are more than two copies on both alleles & ndash; *ultarapid metabolizer* , risk of adverse drug reactions to the metabolite, lack of response to drug
- increased gene expression & ndash; *Ultrarapid Metabolizer* , same as the previous case
- there is one active gene on each allele & ndash; *extensive metabolizer* , normal condition
- one defective allele & ndash; *intermediate metabolizer* , increased drug concentration, decreased metabolite production
- both partially defective alleles & ndash; *intermediate metabolizer* , same as the previous case
- both alleles completely defective & ndash; *poor metabolizer* , very high drug concentration, risk of adverse drug reactions

Drug interactions

Slowing down metabolism

If two different drugs are metabolised by cytochrome P450 and thus *competitively* or *inhibit* each other, their concomitant use may exceed the level they would have if they were taken separately. This is particularly important for drugs with a low therapeutic index [1].



Percentage of cytochromes in drug metabolism

Acceleration of metabolism

It is also often the case that one of the drugs increases the expression of cytochrome P450, so that the other is then metabolised and its concentration decreases. This has been observed, for example, with the concomitant use of some antibiotics and hormonal contraception. In addition, if the metabolic product is a toxic substance, adverse reactions may occur [1].

Substances that increase CYP expression include, for example, environmental pollutants such as cyclic aromatic hydrocarbons and polychlorinated biphenyls.

It also depends on possible liver diseases and other influences.

Links

Source

- ws:Criglerův-Najjarův syndrom

Related Articles

- Biotransformation

Notes

1. This results in a different reactivity, [[Hemoglobin and its derivatives (LF MU) | hemoglobin]] is only a transport protein, cytochromes function as enzymes

External links

- Cytochrom P450 (Czech wikipedia)
- Cytochrome P450 (English wikipedia)

Source

1. VOET, Donald – VOET, Judith G. *Biochemistry.* 3. edition. United States of America : Wiley, John Wiley & Sons, Inc, 2004. 1591 pp. pp. 533–534. ISBN 0-471-19350 - x (cloth) 0-471-39223-5 (Wiley Internation Edition).
2. INGELMAN-SUNDBERG, Magnus – SIM, Sarah C. Pharmacogenetic biomarkers as tools for improved drug therapy; emphasis on the cytochrome P450 system. *Biochemical and Biophysical Research Communications* [online]. 2010, y. 51, vol. 396, no. 1, p. 90-95, Available from <http://www.sciencedirect.com/science/journal/0006291X>. ISSN 0006-291X. PMID: 20494117 (http://www.ncbi.nlm.nih.gov/pubmed/20494117).

Used literature

See references

1. In the Fe $^{2+}$ state with a coordinated CO molecule, they have a characteristic maximum in the absorption spectrum at 450 nm (VOET, Donald – VOET, Judith G. *Biochemistry.* 3. edition. United States of America : Wiley, John Wiley & Sons, Inc, 2004. 1591 pp. pp. 533–534. ISBN 0-471-19350 - x (cloth) 0-471-39223-5 (Wiley Internation Edition).)