

# NO signalling

NO (nitric oxide) is a gas that acts as a **local mediator** in many tissues. It acts only locally because it exists for a very short time (half-life of 5-10 s<sup>[1]</sup>). It reacts with oxygen and water, and changes into nitrates and nitrites. NO has a '**vasodilating effect**' on the smooth muscle of blood vessels. NO is produced by macrophages and neutrophil granulocytes during inflammatory reactions and serves as a cytotoxic tool. NO is used by neurons as a neurotransmitter.

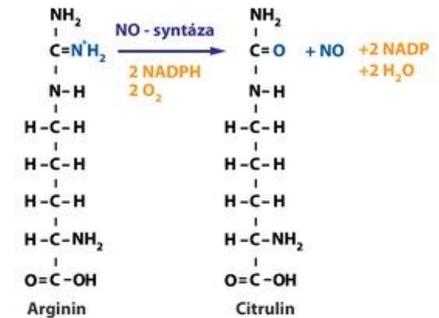
## NO synthesis

It is produced by a group of enzymes called **NO synthases (NOS)**. NOS molecules contain a number of cofactors and prosthetic groups - FMN, FAD, non-heme iron, tetrahydrobiopterin and heme<sup>[2]</sup>. It is derived from the amino acid arginine.

### NO-synthases

There are several isoforms of NOS.

- Constitutive NOS** - Ca<sup>2+</sup> dependent (activated by Ca<sup>2+</sup>):
  - Neuronal NO-synthase (nNOS),
  - Endothelial NO-synthase (eNOS).
- Inducible (also inducible) NOS (iNOS)** - Ca<sup>2+</sup> independent, induced by external signals, expressed by cells of the immune system and endothelium.



NO synthesis

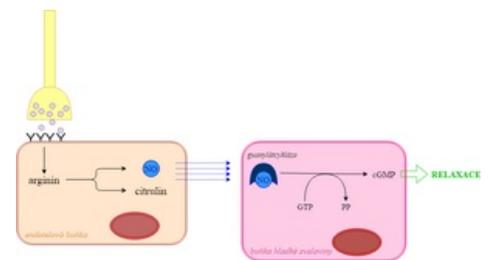
## General mechanism of action of NO

NO does not act on the cell that produces it, but on surrounding cells.

- 1. cell** synthesizes NO, which then diffuses cytoplasmic membrane into the other cell.
- 2. the cell** receives NO, which binds to soluble guanylate cyclase in it, causing an increase in cGMP concentration. An increased concentration of cGMP starts a cascade of events that results in the dilation of the given cell. The resulting effect is vasodilation in the vascular bed.

## The role of NO in the relaxation of smooth muscle in the vascular wall

Endothelial cells constantly produce a small amount of nitric oxide that keeps blood flowing through the vessels. However, if vasodilation is to occur, endothelial cells release NO in response to nerve stimulation. NO freely passes through the membrane (diffuses) from the endothelial cell, in which it is synthesized, into the smooth muscle cell. Inside the smooth muscle cell, NO binds to the enzyme 'soluble guanylate cyclase' located in the cytosol. Subsequently, the formation of 'cGMP' occurs from GTP. cGMP is a second messenger that activates protein kinase G, and through the phosphorylation of various proteins, the intracellular concentration of Ca<sup>2+</sup> will decrease and the smooth muscle cell will relax.



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## Role of NO in erection

NO is released by nerve endings in the penis and causes blood vessels to dilate, which is responsible for an erection. When sexual arousal decreases, cGMP is rapidly broken down to GMP by the action of cGMP-specific phosphodiesterase. Viagra and related drugs slow the breakdown of cGMP and thus maintain an erection.<sup>[1]</sup>

## References

### Related articles

- Cell Signaling
- Nitric Oxide
- Nitric Oxides
- Arginine

### Source

- ŠEDO, Prof. MUDr. Aleksí. *Signální transdukce III* [lecture for subject Lékařská chemie a biochemie 1, specialization Biochemie, 1.LF UK]. Praha. 13.1.2016.

## References

1. KOOLMAN, Jan – RÖHM, Klaus-Heinrich. *Barevný atlas biochemie*. 1. edition. Praha : Grada, 2012. 512 pp. ISBN 978-80-247-2977-0.
2. MATOUŠ, Bohuslav, et al. *Základy lékařské chemie a biochemie*. 1. edition. Prague : Galén, 2010. 540 pp. ISBN 978-80-7262-702-8.

## References used

- MATOUŠ, Bohuslav, et al. *Základy lékařské chemie a biochemie*. 1. edition. Praha : Galén, 2010. 540 pp. ISBN 978-80-7262-702-8.
- BRUCE, Alberts – BRAY, D – JOHNSON, A, et al. *Základy buněčné biologie*. 1. edition. Ústí nad Labem : Espero Publishing, 1998. 630 pp. ISBN 80-902906-0-4.
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