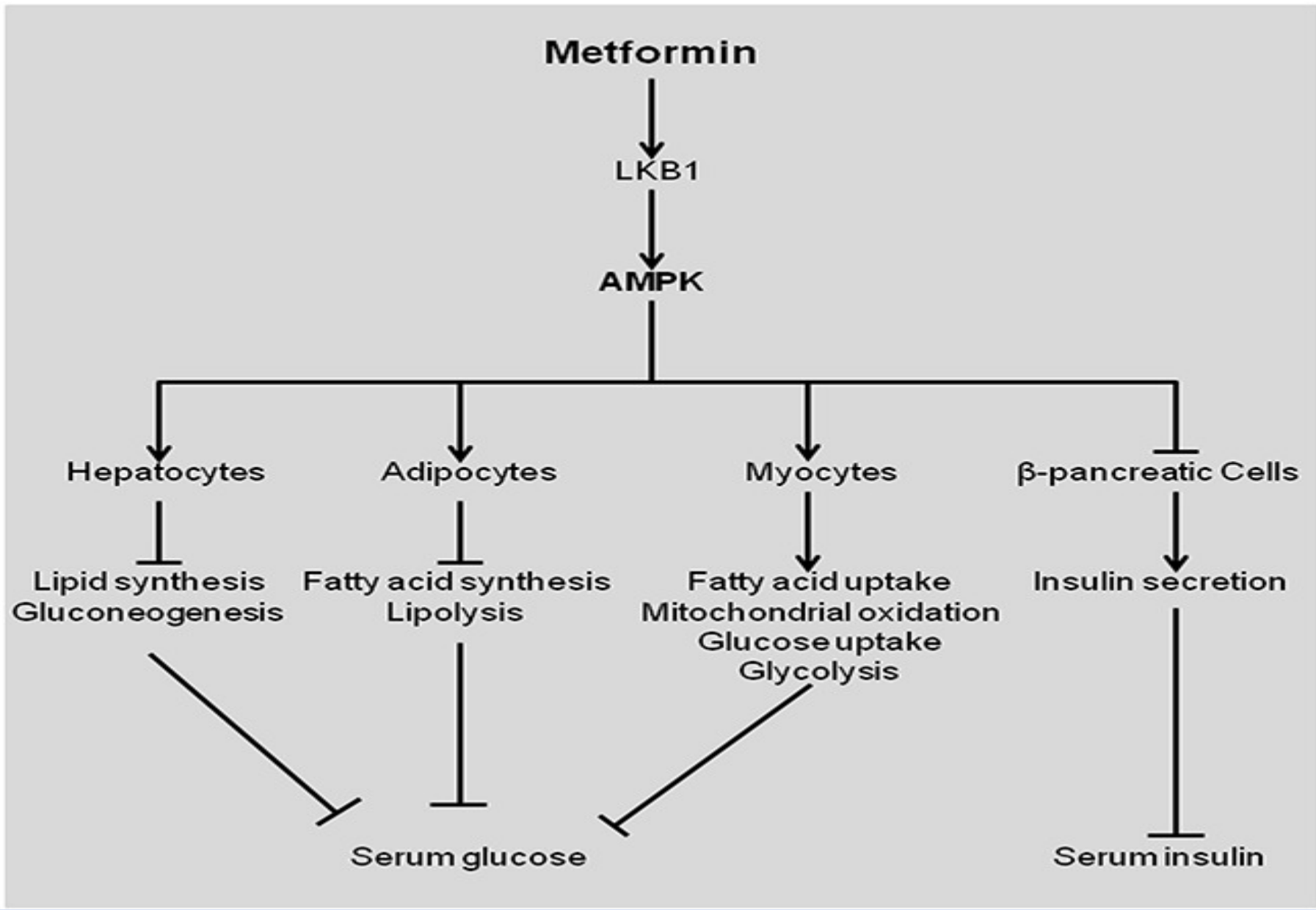
INSULIN SENSITIZERS:
Metformin

Prof.Dr.Nuray Arı, 2018


THE MANY BENEFITS OF METFORMIN

Established clinical applications of metformin other than type 2 diabetes

- ***Prediabetes***
- ***Insulin resistance and metabolic syndrome***
- ***Polycystic ovary syndrome***

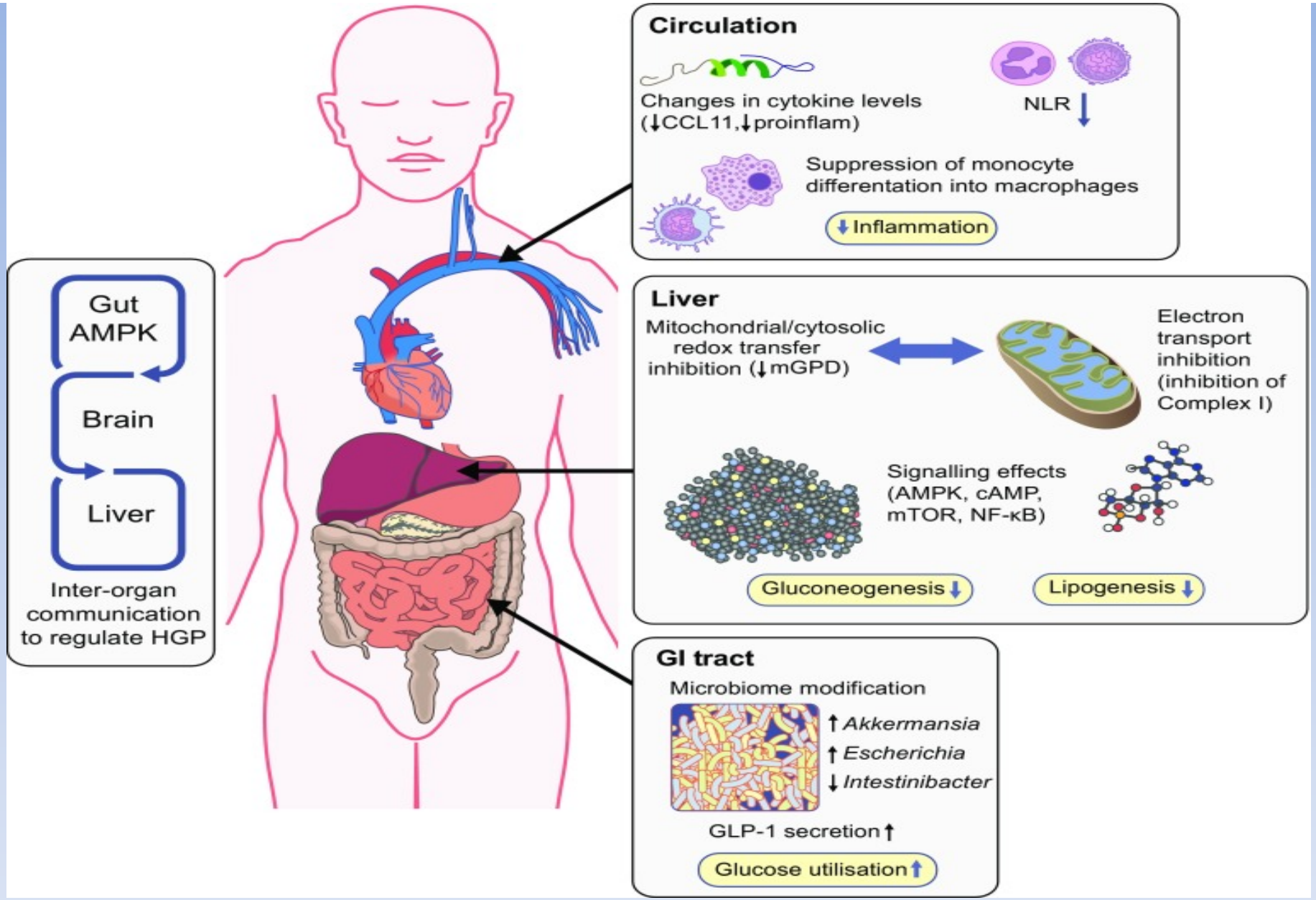


Effects of metformin in patients with diabetes type 2.

Oncotarget. 2017 17;8(3):5619-5628. **Anti-tumor activity of metformin: from metabolic and epigenetic perspectives.** Yu X al.

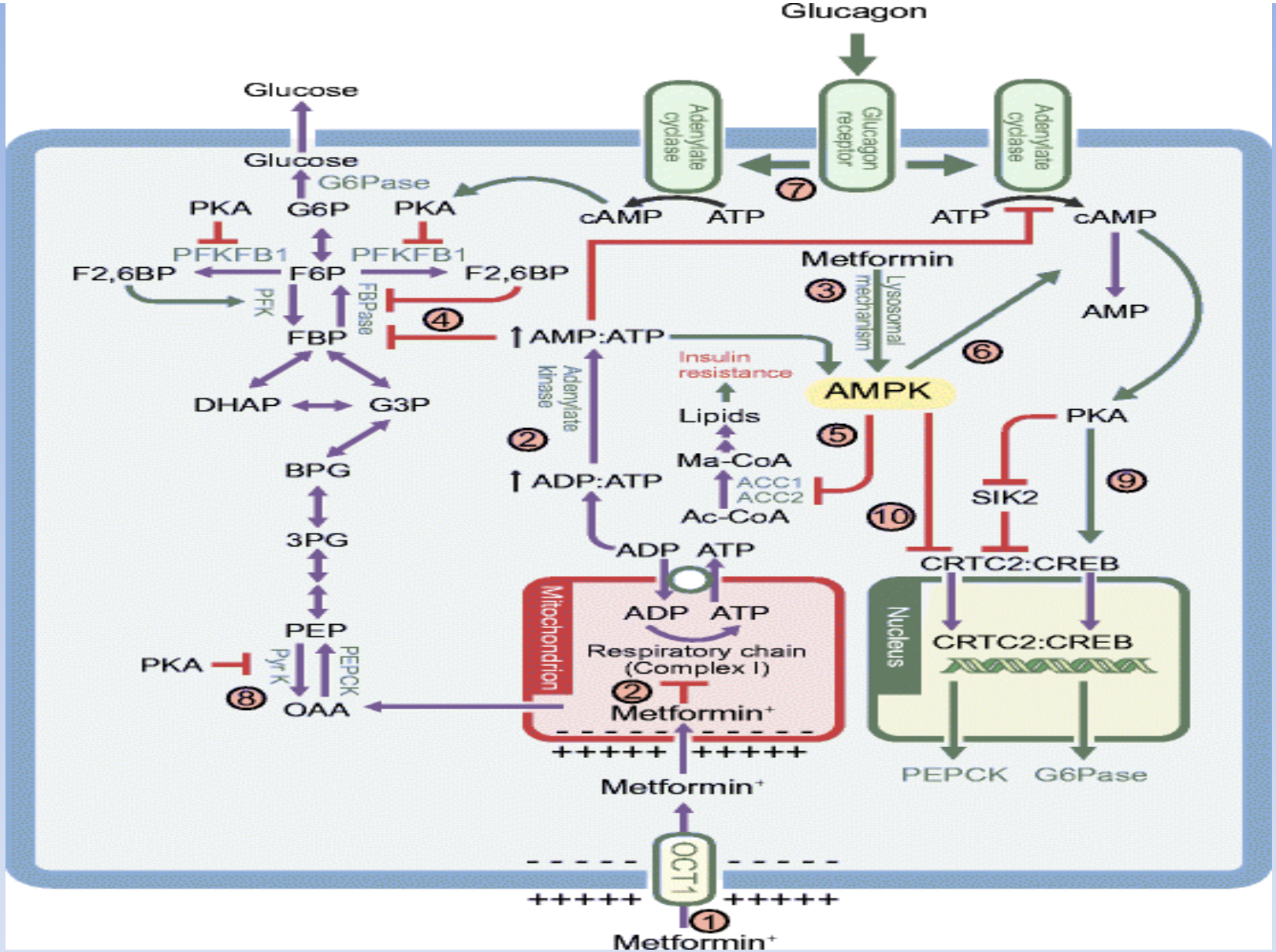
- *Diabetologia. 2017 Sep;60(9):1577-1585. doi: 10.1007/s00125-017-4342-z. Epub 2017 Aug 3.*
- **The mechanisms of action of metformin.**
- Rena G, Hardie DG, Pearson ER.

- **Abstract**
- **Metformin is a widely-used drug that results in clear benefits in relation to glucose metabolism and diabetes-related complications. The mechanisms underlying these benefits are complex and still not fully understood. Physiologically, metformin has been shown to reduce hepatic glucose production, yet not all of its effects can be explained by this mechanism and there is increasing evidence of a key role for the gut. At the molecular level the findings vary depending on the doses of metformin used and duration of treatment, with clear differences between acute and chronic administration. Metformin has been shown to act via both AMP-activated protein kinase (AMPK)-dependent and AMPK-independent mechanisms; by inhibition of mitochondrial respiration but also perhaps by inhibition of mitochondrial glycerophosphate dehydrogenase, and a mechanism involving the lysosome. In the last 10 years, we have moved from a simple picture, that metforminimproves glycaemia by acting on the liver via AMPK activation, to a much more complex picture reflecting its multiple modes of action. More work is required to truly understand how this drug works in its target population: individuals with type 2 diabetes.**



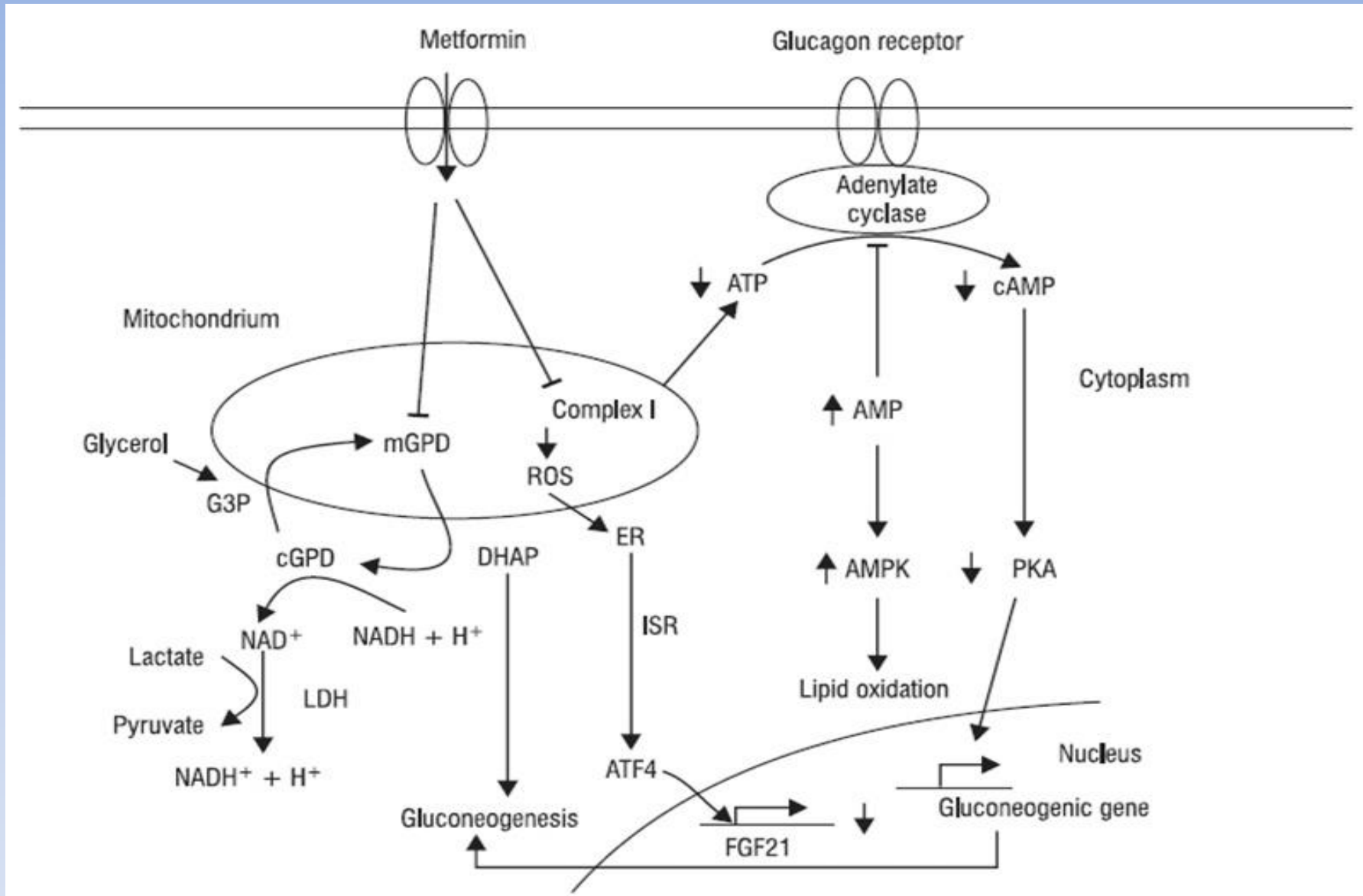
Actions of metformin on metabolism and inflammation .

Diabetologia. 2017 Sep;60(9) :1577-1585. **The mechanisms of action of metformin.** Rena G et al.



The multiple mechanism via which metformin affects liver metabolism.

Diabetologia. 2017 Sep;60(9):1577-1585 **The mechanisms of action of metformin.** Rena G et al.

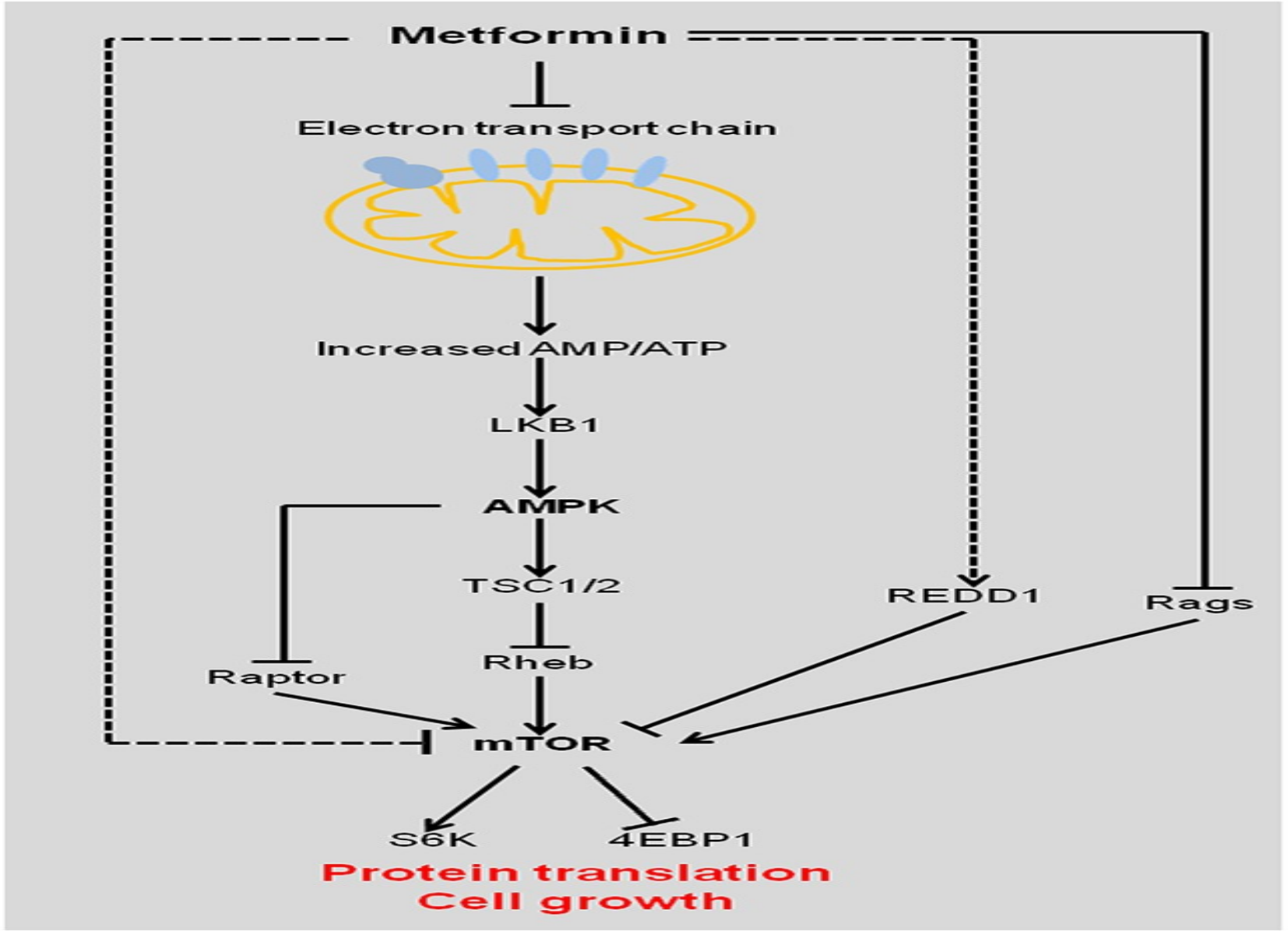


Mechanisms of metformin action

Endokrynol Pol. 2017;68(4):482-496. **Metformin - a new old drug.** Wróbel M et al.

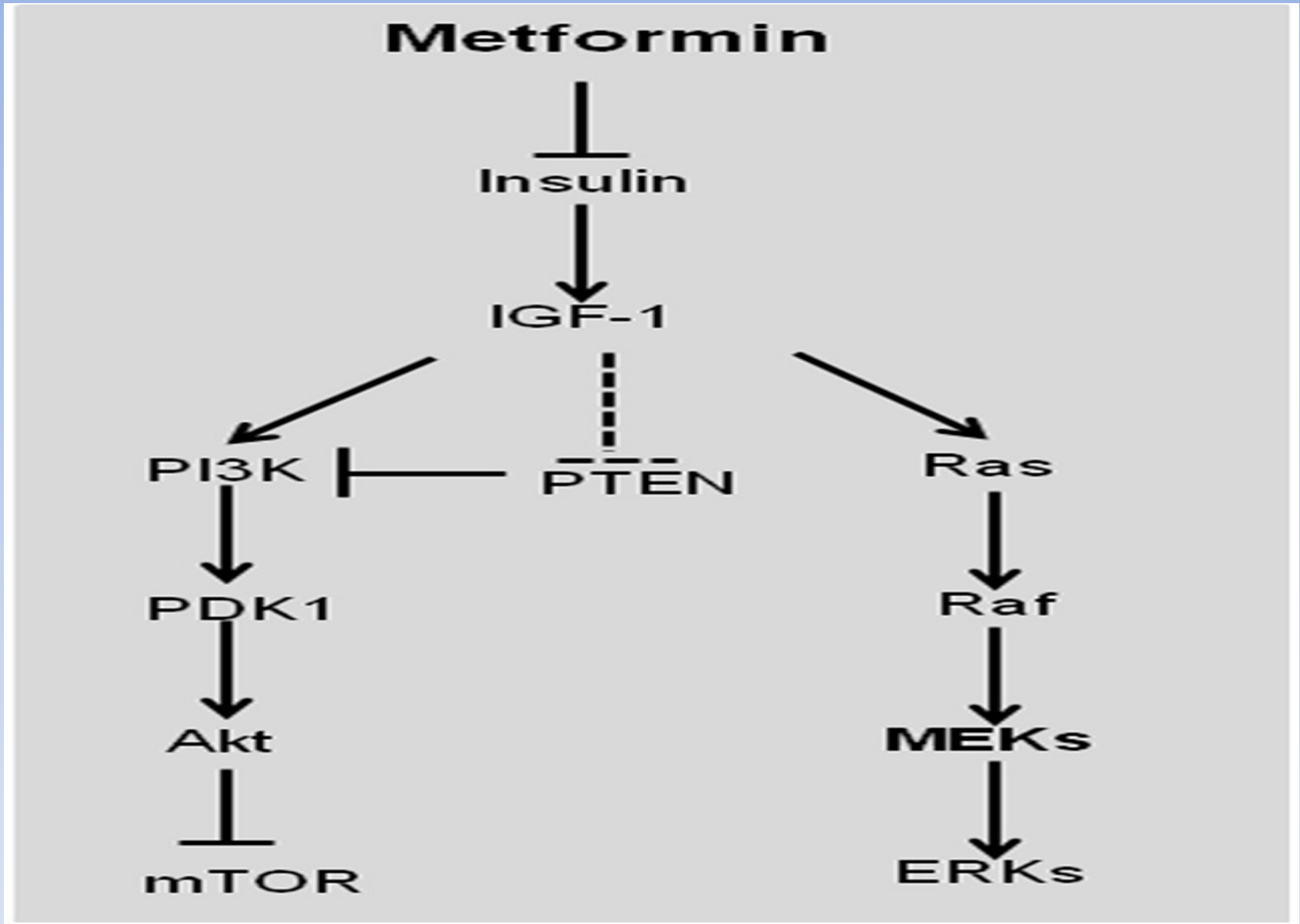
- Oncotarget. 2017 Jan 17;8(3):5619-5628. doi: 10.18632/oncotarget.13639.
- **Anti-tumor activity of metformin: from metabolic and epigenetic perspectives.**
- Yu X, Mao W, Zhai Y, Tong C, Liu M, Ma L, Yu X, Li S.

- **Abstract**
- **Metformin has been used to treat type 2 diabetes for over 50 years. Epidemiological, preclinical and clinical studies suggest that metformintreatment reduces cancer incidence in diabetes patients. Due to its potential as an anti-cancer agent and its low cost, metformin has gained intense research interest. Its traditional anti-cancer mechanisms involve both indirect and direct insulin-dependent pathways. Here, we discussed the anti-tumor mechanism of metformin from the aspects of cell metabolism and epigenetic modifications. The effects of metforminon anti-cancer immunity and apoptosis were also described. Understanding these mechanisms will shed lights on application of metformin in clinical trials and development of anti-cancer therapy.**



INDIRECT effect of metformin in suppressing tumorigenesis

Oncotarget. 2017 17;8(3):5619-5628. **Anti-tumor activity of metformin: from metabolic and epigenetic perspectives.** Yu X et al.



Schematic representation of the DIRECT effect of metformin in suppressing tumorigenesis. Oncotarget. 2017 17;8(3):5619-5628. **Anti-tumor activity of metformin: from metabolic and epigenetic perspectives.** Yu X et al.