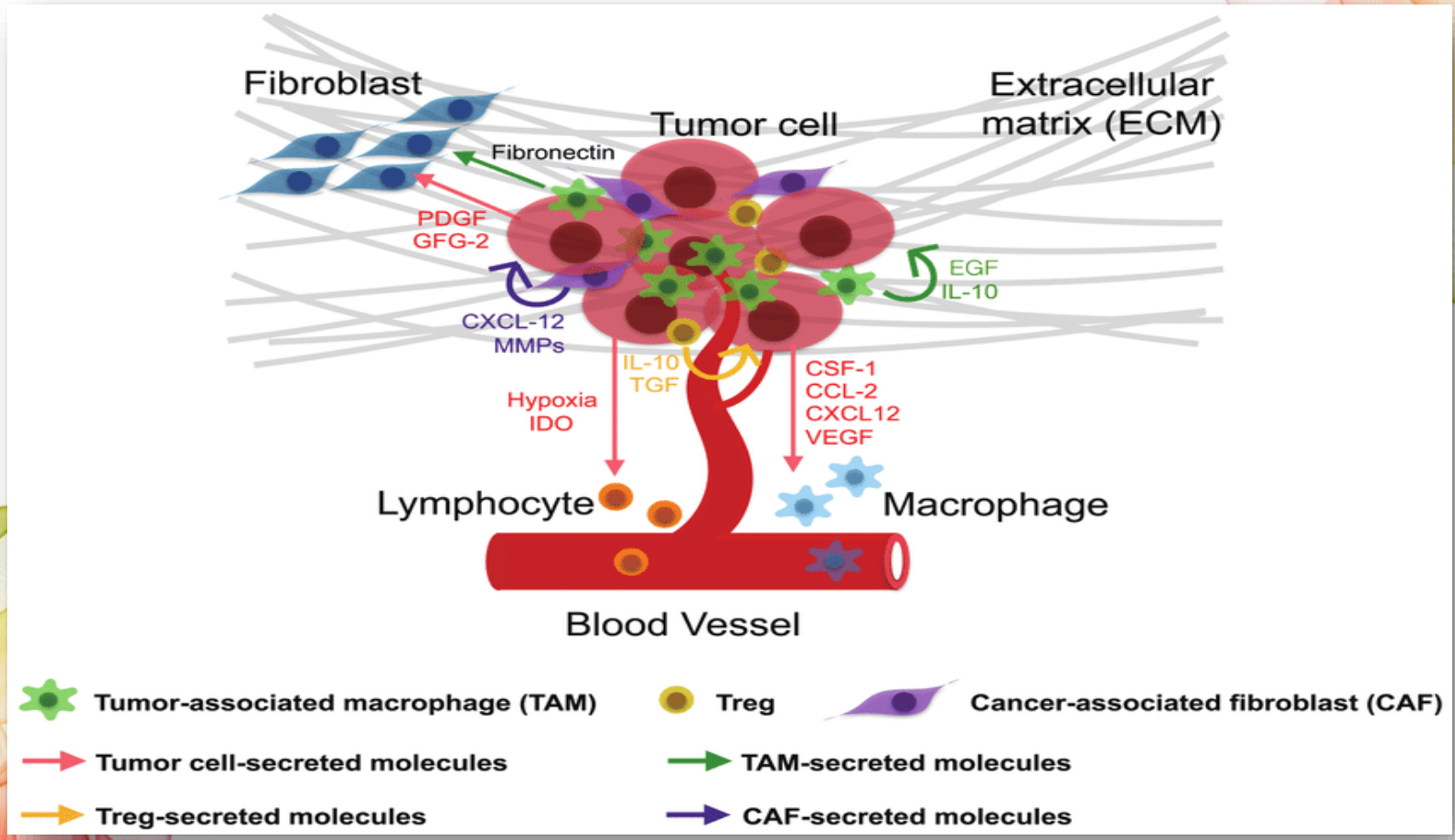
بسم الله الرحمن الرحيم

Role of the BM microenvironment in drug resistance of hematological malignances

Mohammd khani-Eshratabadi

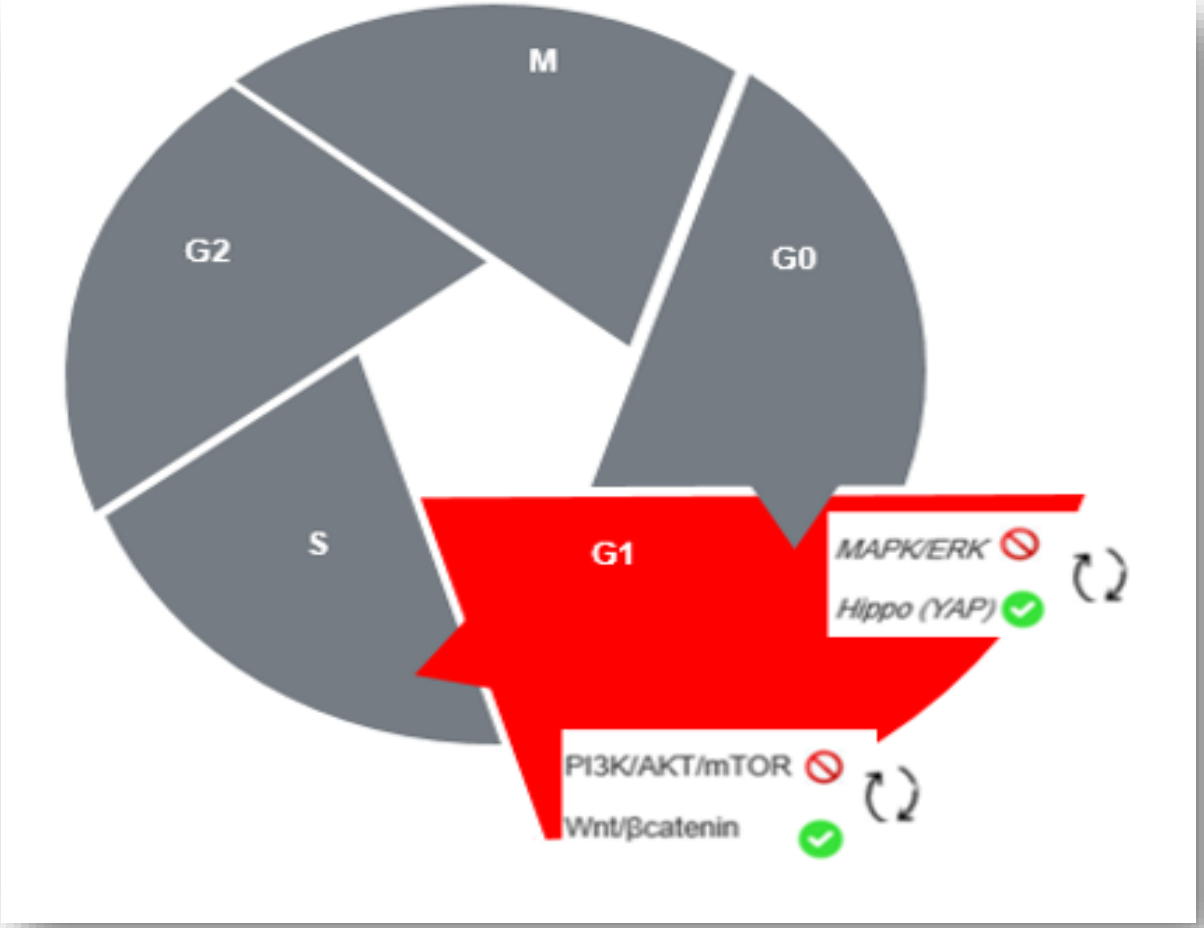
Introduction

Tumor microenvironment components

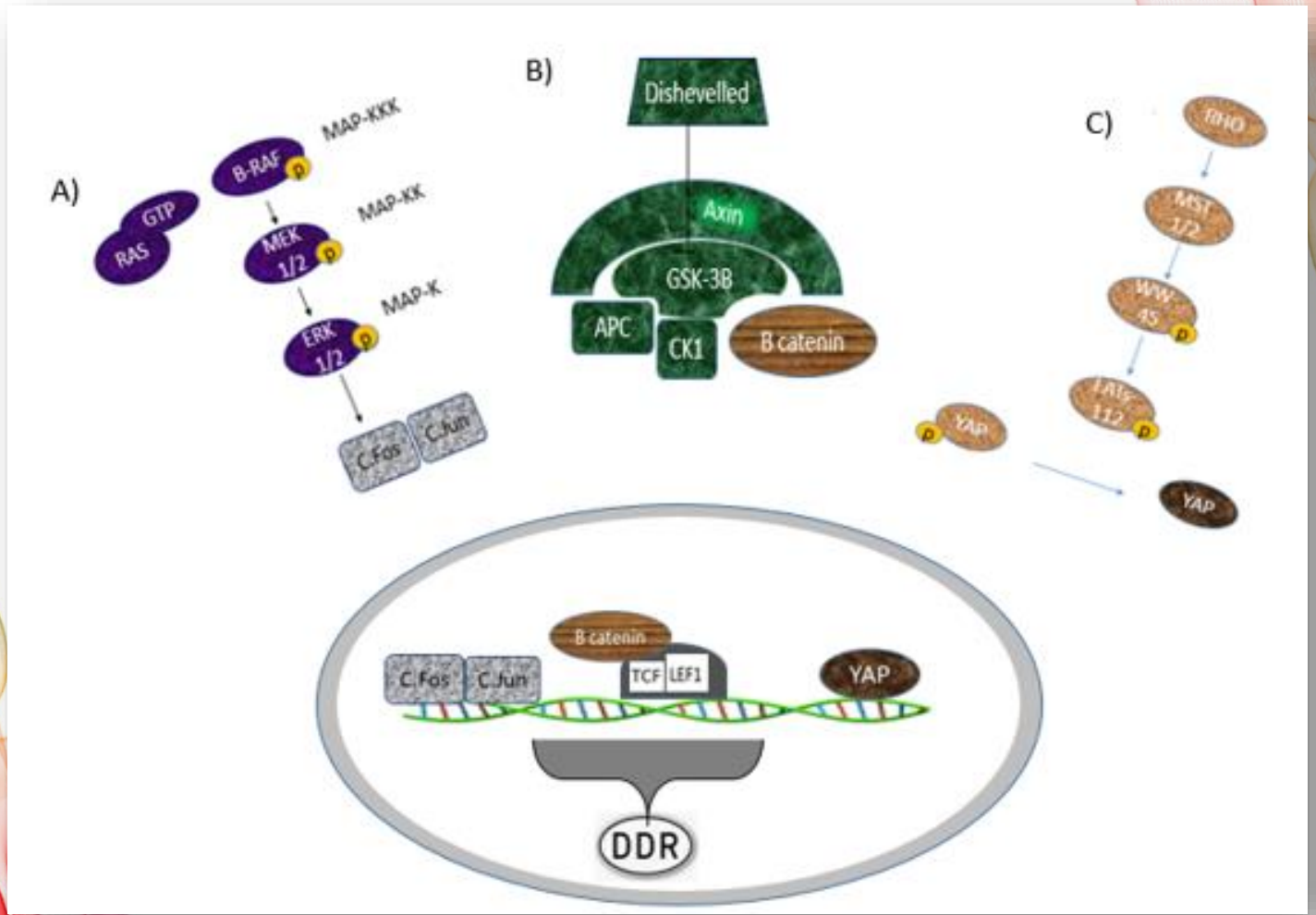


Signaling pathways and drug resistance

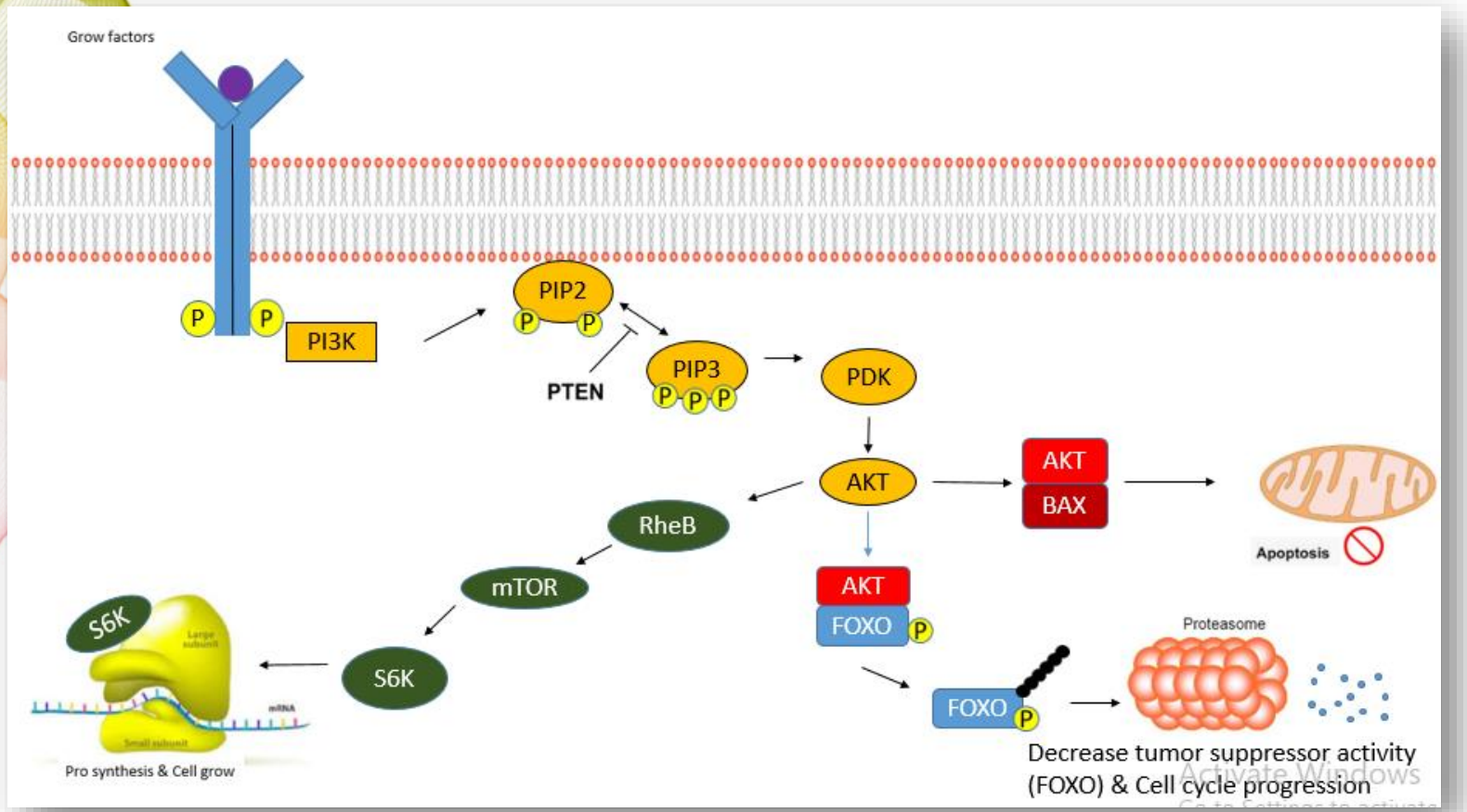
Cell cycle pathways involved in DR



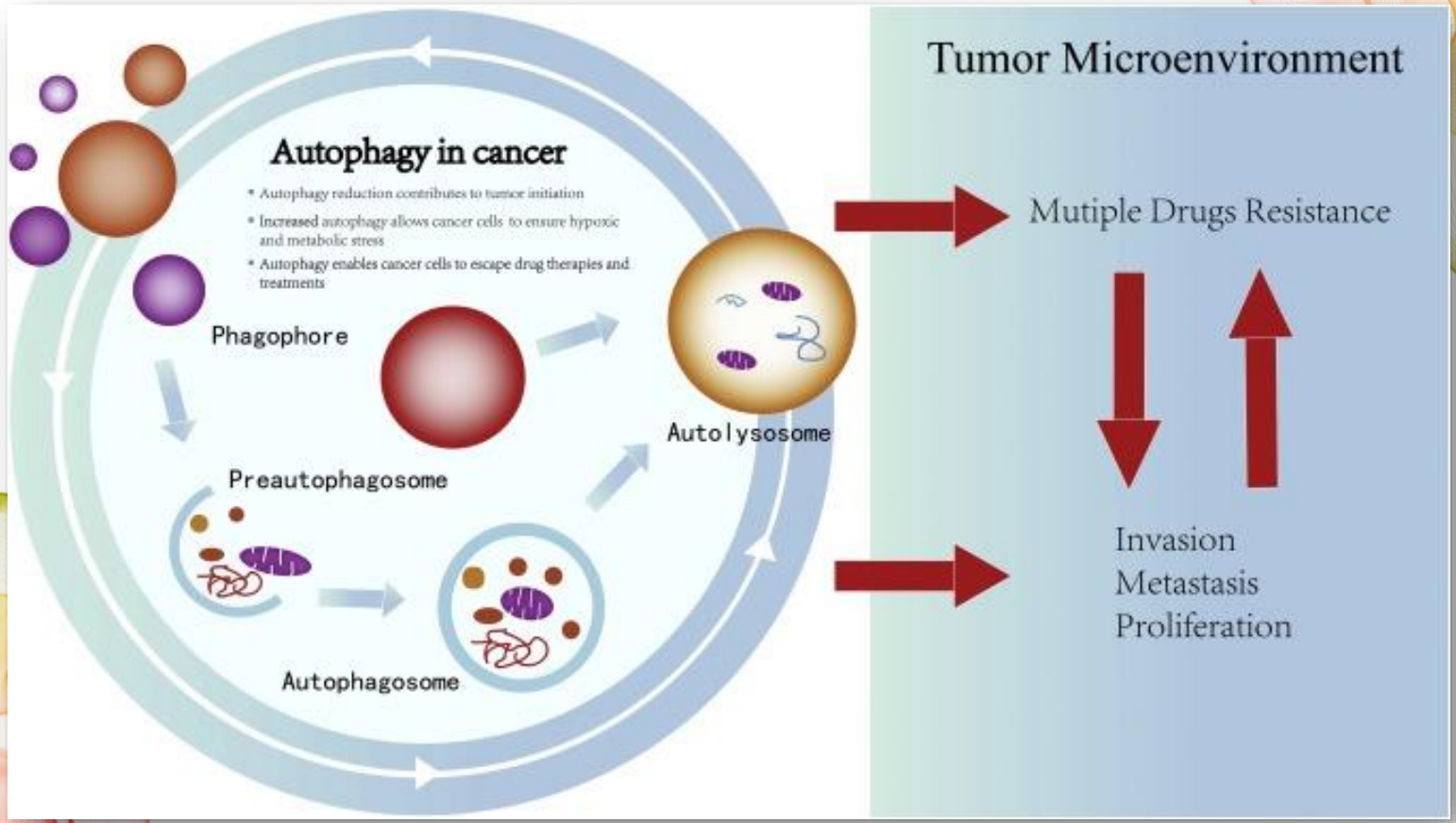
3 main pathways involved in tumor cell growth, proliferation and DR



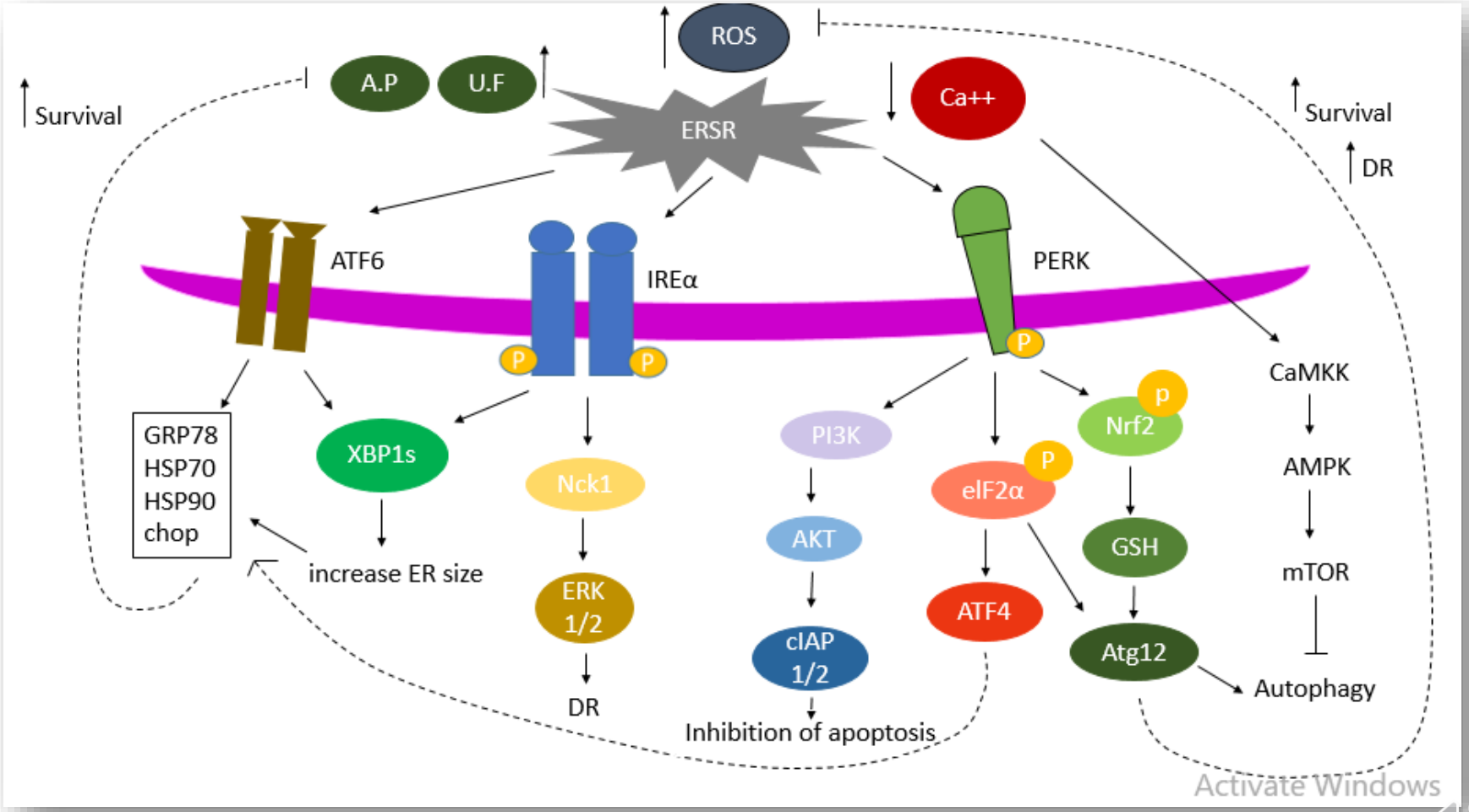
Secondary pathways can compensate for the inhibition of primary pathways to produce DR



Autophagy


Autophagy in cancer
Autophagy reduction contributes to tumor initiation
Increased autophagy allows cancer cells to ensure hypoxic and metabolic stress
Autophagy enables cancer cells to escape drug therapies and treatments
Phagophore
Autolysosome
Preautophagosome
Autophagosome
Tumor Microenvironment
Mutiple Drugs Resistance
Invasion
Metastasis
Proliferation

Stress pathways, autophagy and malignant fitness



Discussion and conclusion

↑ activity of alternative pathways after inhibiting the primary pathway by chem otherapy drugs → development of DR.

Thus, tumor cells can find a way to survive (effective chemotherapy regimens)

→  alternative pathways could be effective in overcoming DR.

→ The role of TME components in activating autophagy is undeniable.

ex

Changes in the expression of anti-apoptosis genes

increase in cell cycle checkpoints to repair drug-induced DNA damage.

Autophagy (dual function) → inducing DR and increasing invasion → ↓ effectiveness of chemotherapy drugs ⇆ type 2 cell death and kill malignant cells that are resistant to apoptosis.

ERSR → 3 sensors of ATF6, IRE1 and PERK → reducing unfolded proteins b y chaperone activity → increase DR and tumor survival.

use of inhibitors of ERSR

سپاس از توجه شما

آخرین زمستان قرن ۱۴- کاشمر