NOUVEAU MECANISME D'ACTION DES VINCA ALCALOÏDES DANS DES CELLULES DE NEUROBLASTOME HUMAIN; IMPLICATION DE LA MITOCHONDRIE

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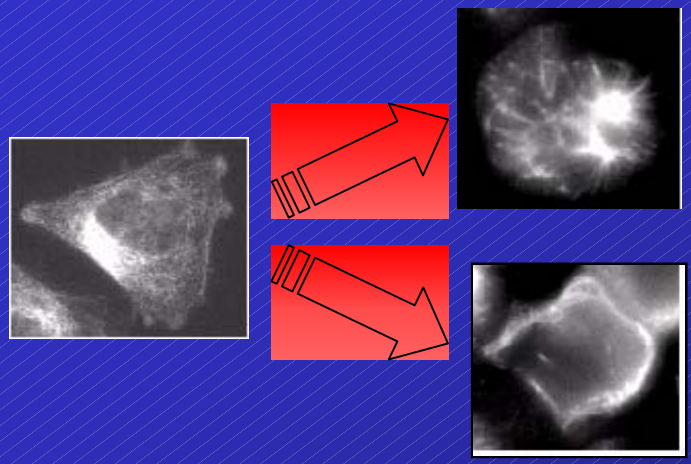
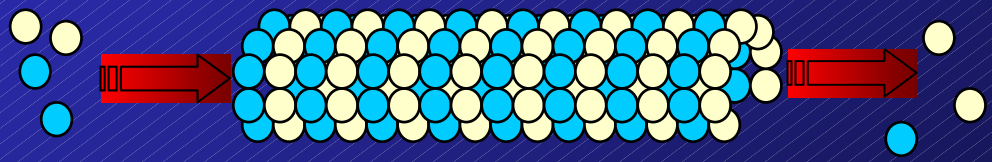
ANTI-MITOTIQUES

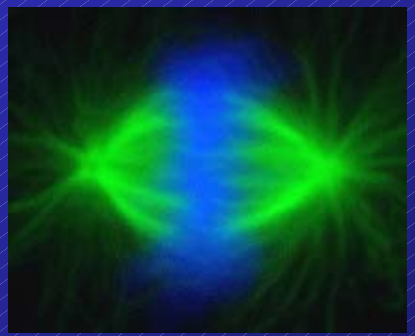
•agents anti-tubuline

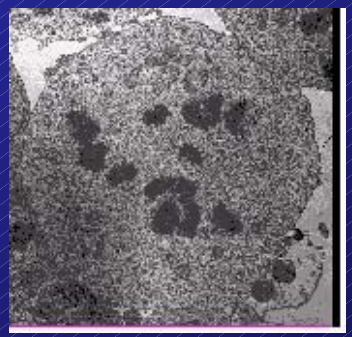


• diminuent la dynamique des microtubules

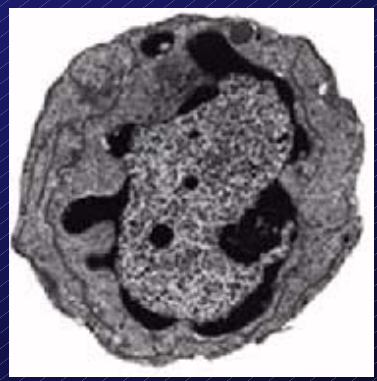


• induisent un blocage en mitose

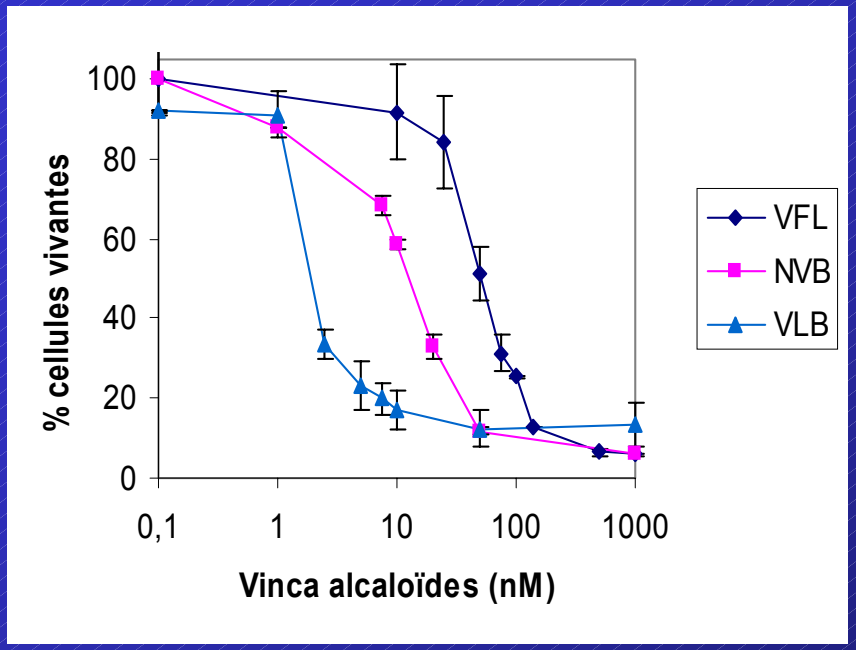


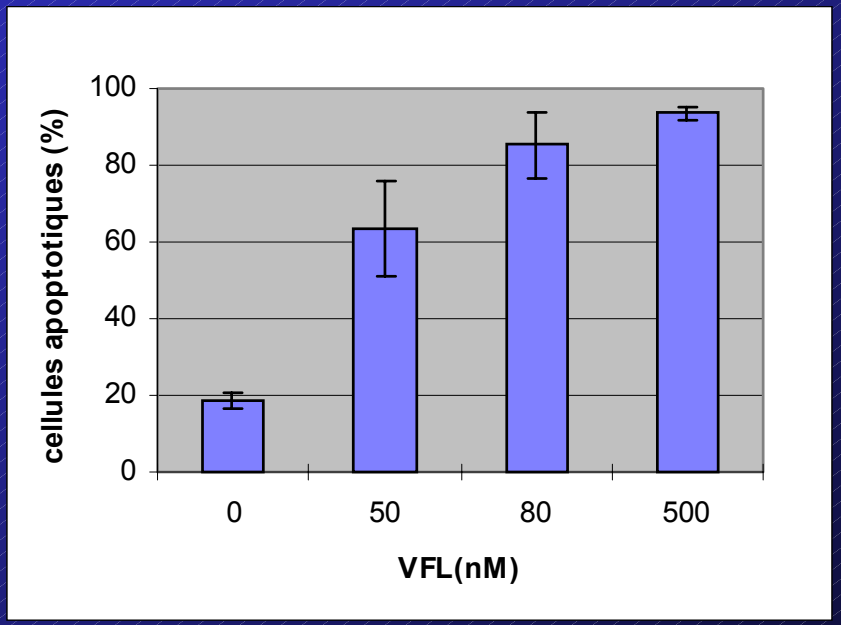


• entraînent l 'apoptose



CYTOTOXICITE DES VINCA-ALCALOIDES SUR SK-N-SH

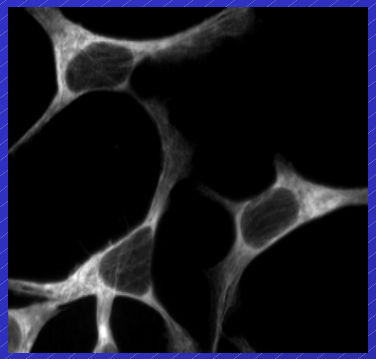


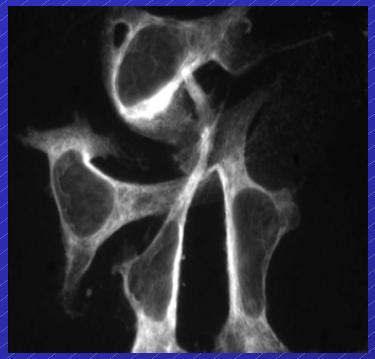


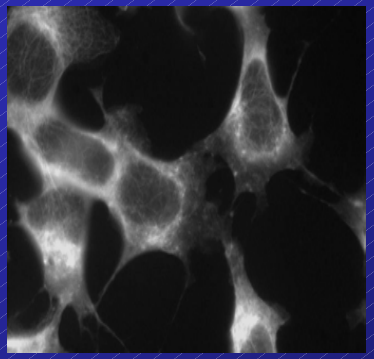
	IC_{50}	IC_{70}
Vinblastine (VLB)	2 nM	4 nM
Vinorelbine (NVB)	13 nM	30 nM
Vinflunine (VFL)	50 nM	80 nM

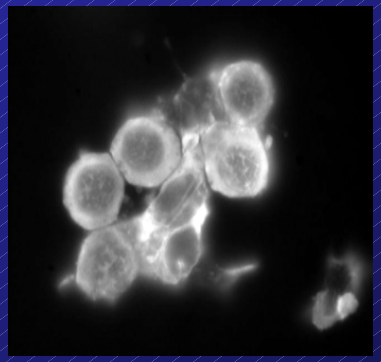
Apoptose massive

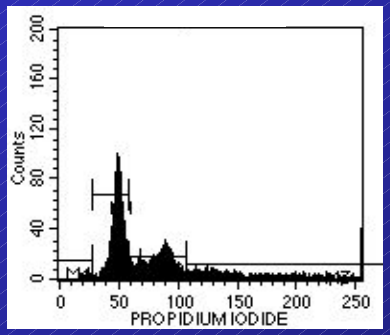
RESEAU MICROTUBULAIRE ET BLOCAGE EN MITOSE

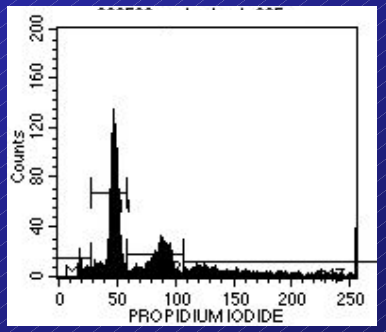

Contrôle

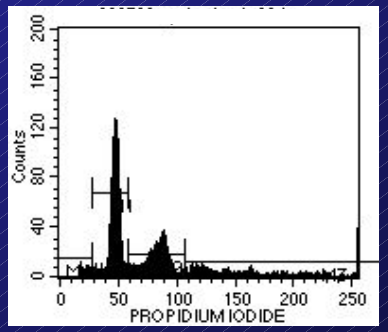

NVB IC_{50}

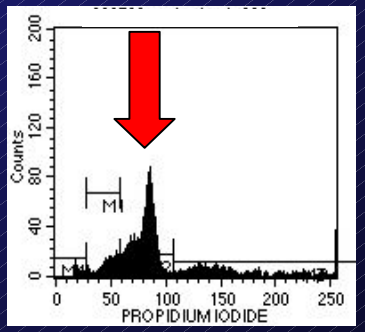

NVB IC_{70}


NVB 500nM



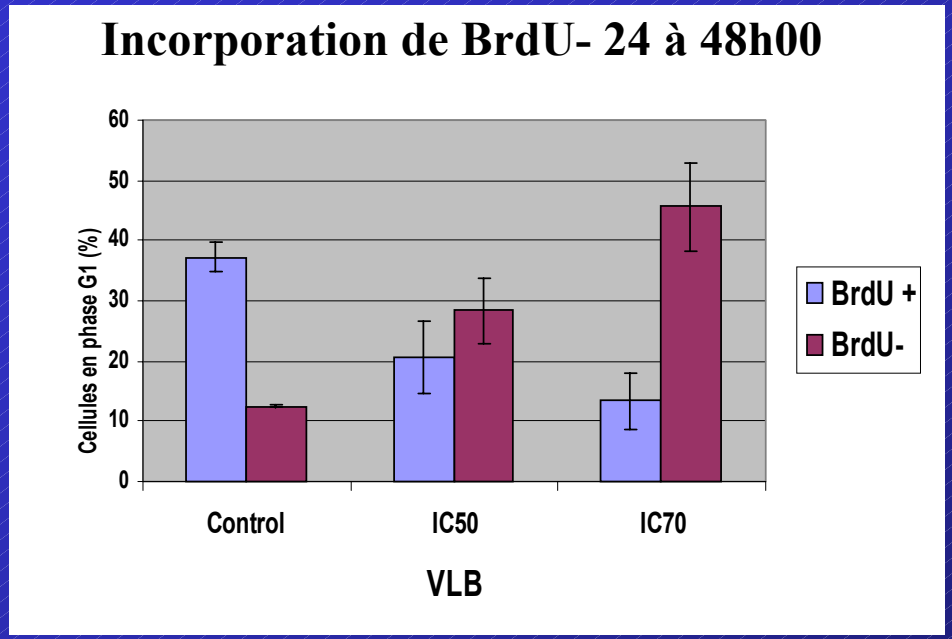


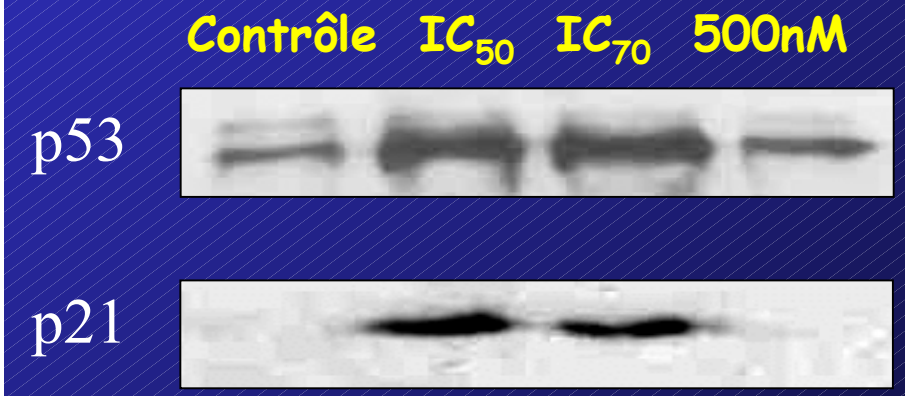




Dépolymérisation massive et blocage en mitose uniquement pour les fortes concentrations

Et les faibles doses???



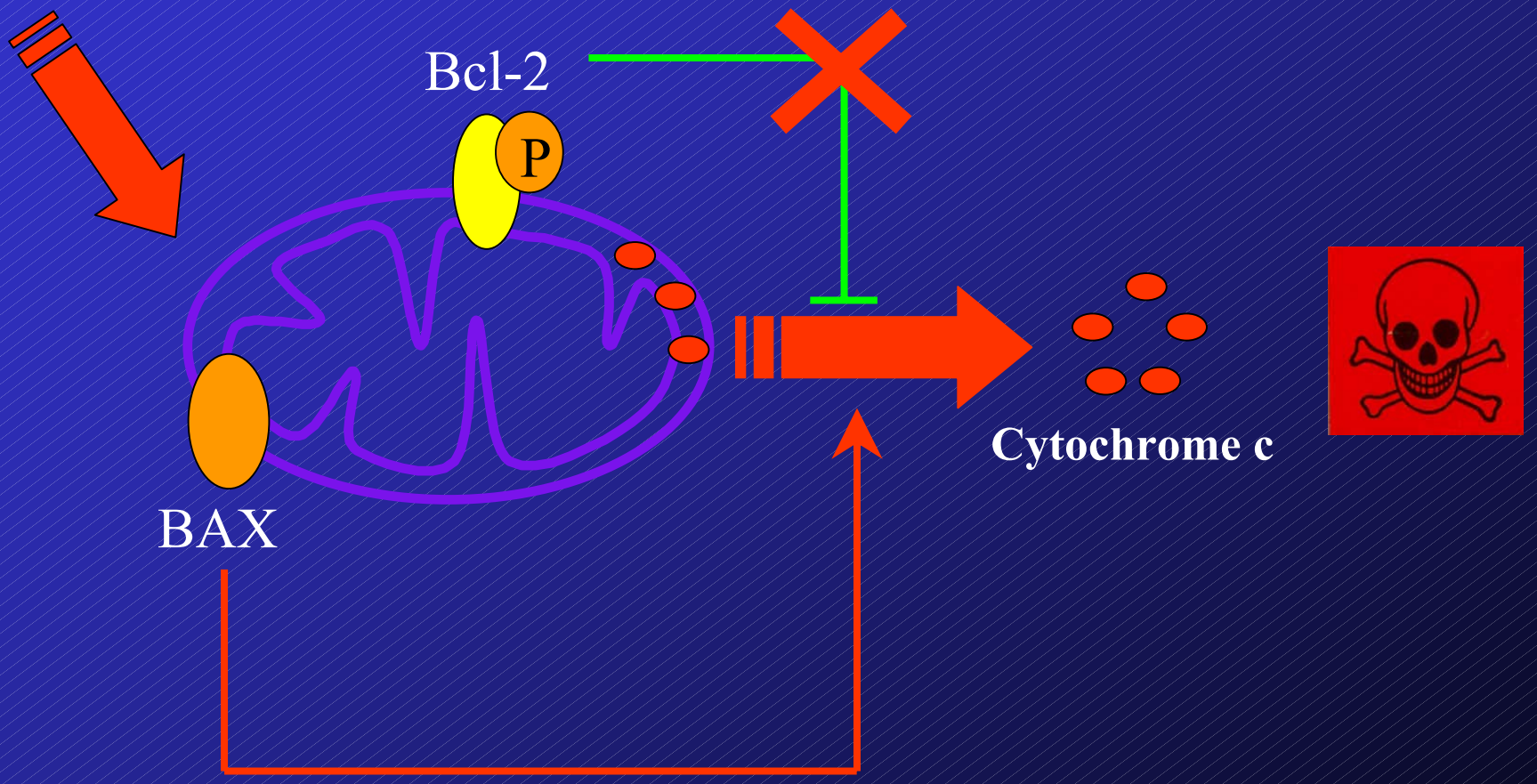


Blocage en phase G1

Induction de p53 et de sa cible p21

ARRÊT EN PHASE G1, p53 DEPENDANT

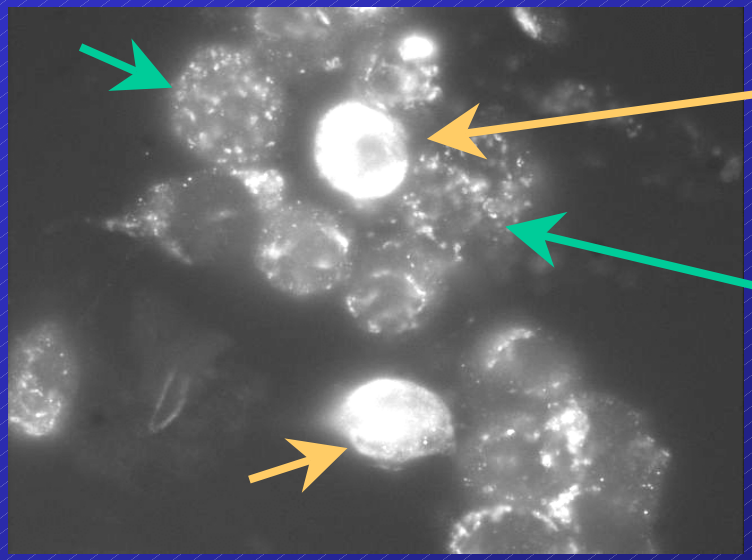
MITOCHONDRIE ET APOPTOSE



IMPLICATION DE LA MITOCHONDRIE ?
MODULATION DIFFERENTE?

RÔLE DE LA MITOCHONDRIE

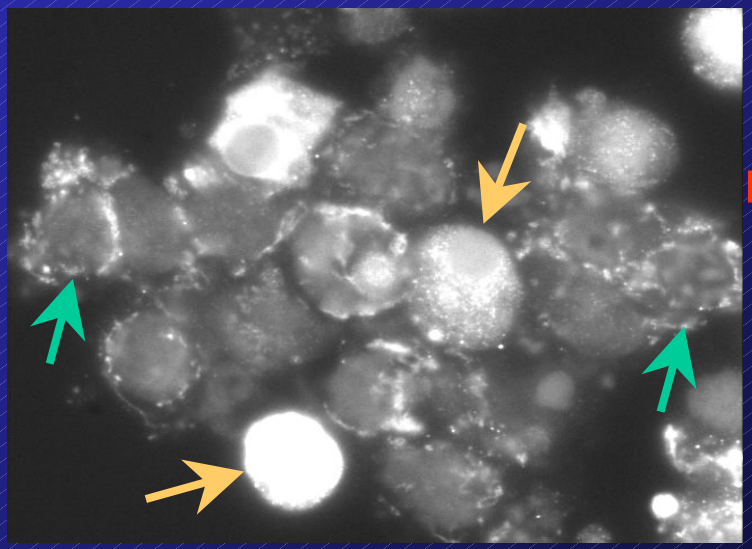
VLB IC_{50}



Cytochrome c libéré

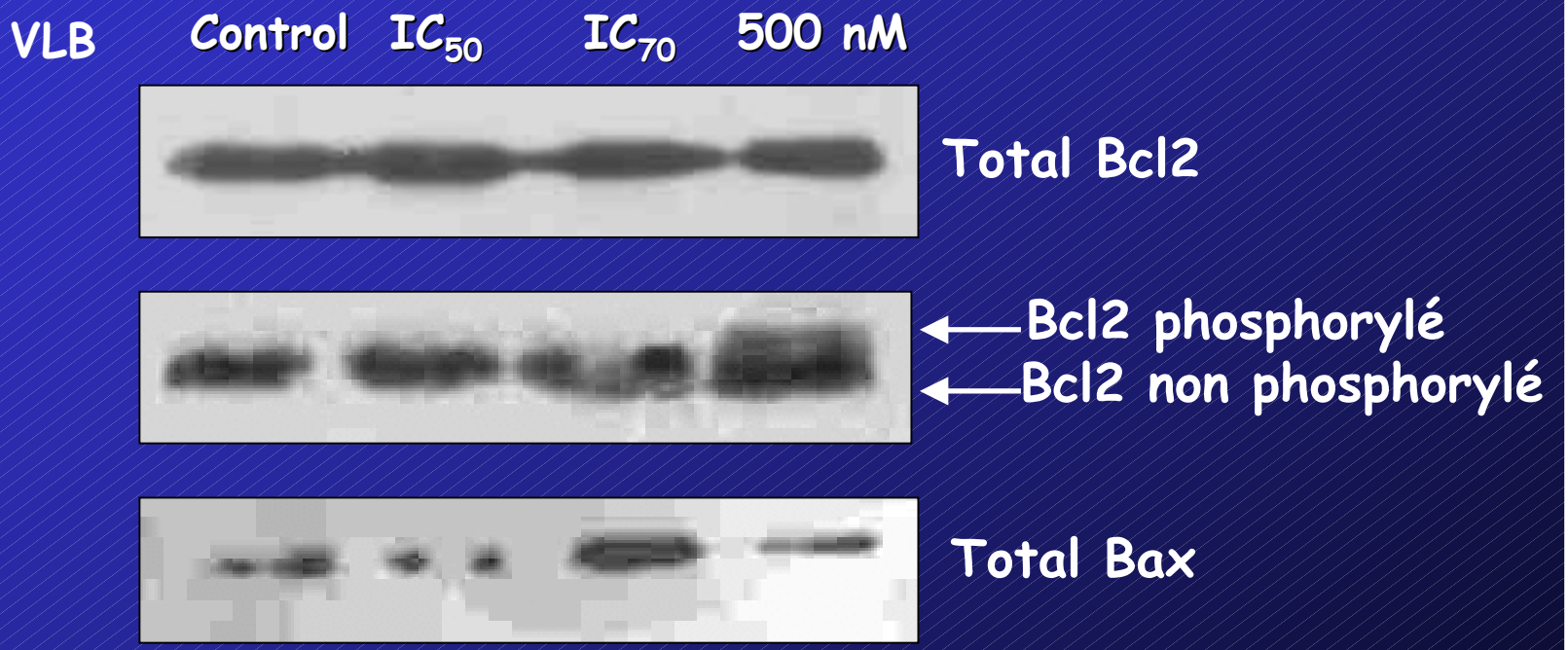
Cytochrome c non libéré

VLB 500nM



Implication de la mitochondrie pour toutes les concentrations testées

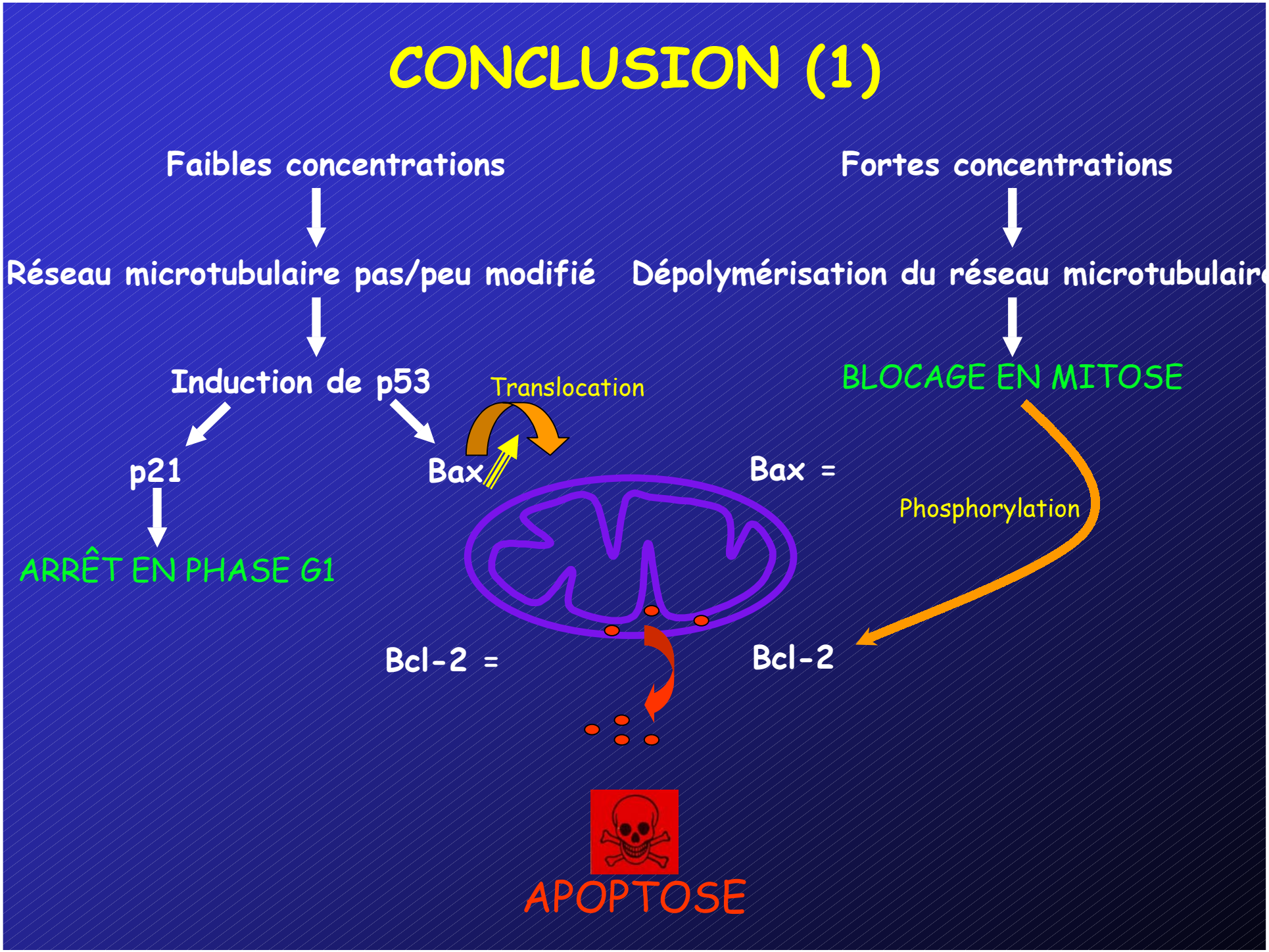
RÔLE DE BAX ET Bcl-2



Mitochondrie point de convergence

Modulation différente en fonction de la concentration

CONCLUSION (1)



CONCLUSION (2)

- Nouveau mécanisme d'action des Vinca-alcaloïdes
- Faibles concentrations actives
- Spécificité de lignée ?
  - Voies de signalisation spécifiques
  - Nouvelle cible thérapeutique
  - Validation sur modèle animal
  - Essais cliniques

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