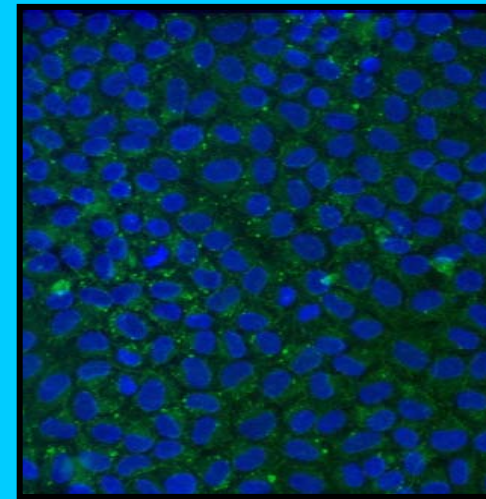


Buněčné kultury jako nástroj pro studium toxických látek znečišťujících životní prostředí



Biofyzikální ústav AV ČR, v.v.i., Brno

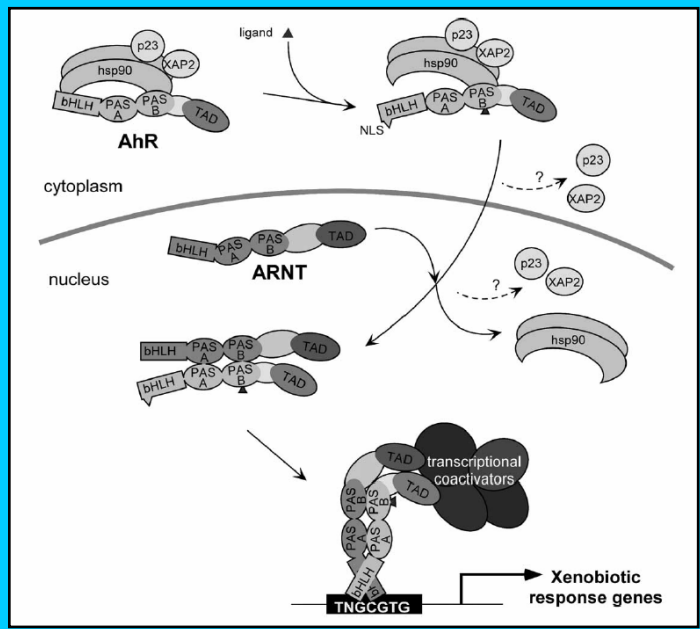
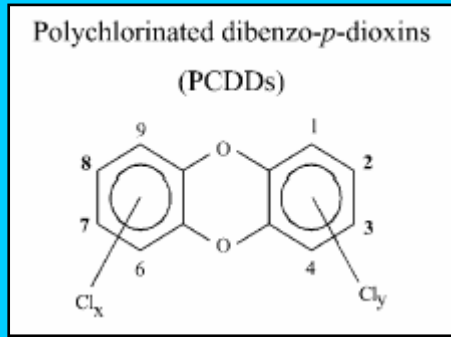
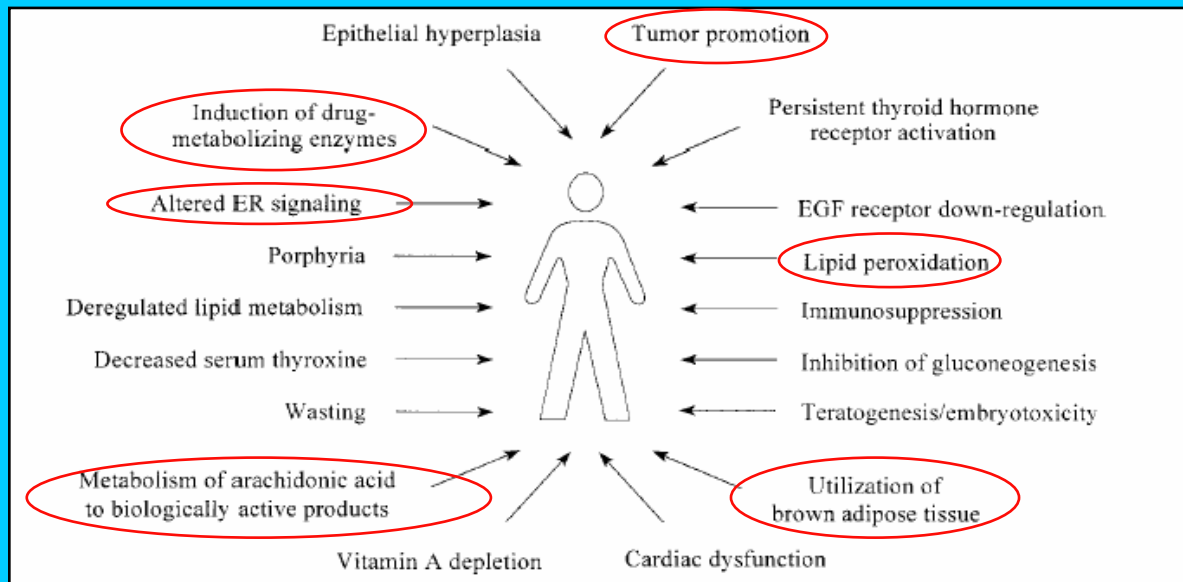


Jan Vondráček
Skupina buněčné a molekulární toxikologie
Oddělení cytokinetiky
Biofyzikální ústav AV ČR, v.v.i.



vondracek@ibp.cz; <http://www.ibp.cz/labs/LC/>

Activace a účinky AhR:



„Classical“ AhR-regulated genes:

contain xenobiotic response elements (XRE) or dioxin responsive elements (DRE) in their promoter region:

- phase I and II enzymes - *CYP1A1*, *CYP1A2*, *CYP1B1*, *UDP-glucuronosyltransferase*, *GST-Ya*, *NQO1*;
- AhRR.

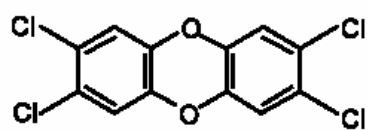


AhR-regulated genes involved in control of cell proliferation and cell death:

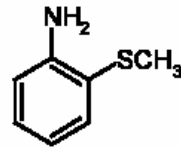
- pro-apoptotic genes - *Bax*;
- immediate - early response genes - *Jun*, *Fos*;
- cell cycle regulation - *p27^{Kip1}*, *p21^{Waf/Cip}*.

„Non-classical“ AhR ligands

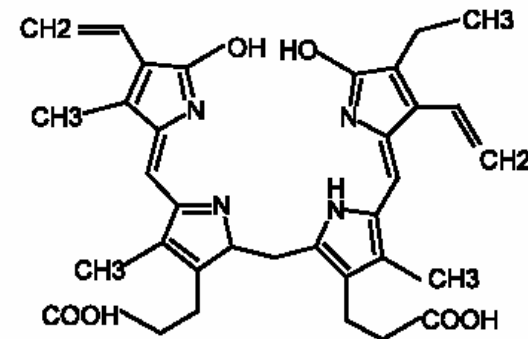
M.S. Denison et al. / Chemico-Biological Interactions 141 (2002) 3–24



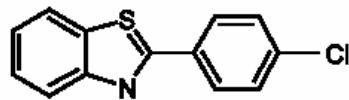
2,3,7,8-Tetrachlorodibenzo-p-dioxin



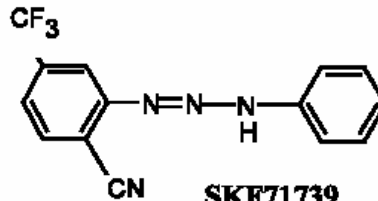
2-(Methylmercapto)aniline



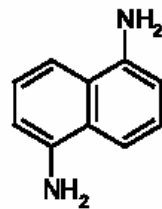
Bilirubin



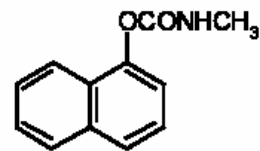
2-(4'-Chlorophenyl)benzothiazole



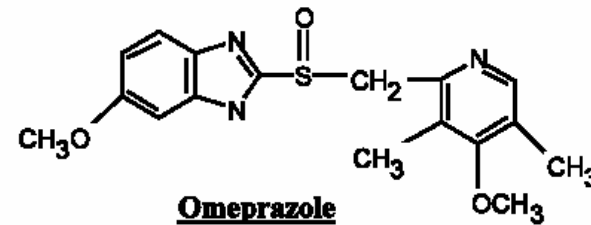
SKF71739



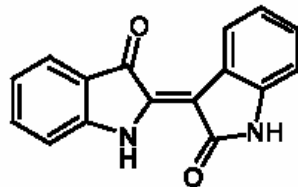
1,5-Diaminonaphthalene



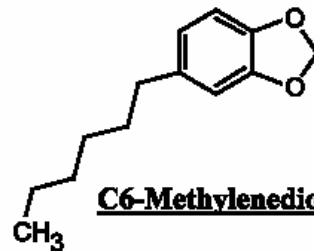
Carbaryl



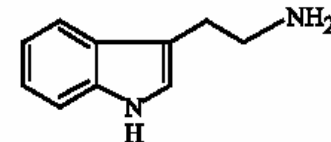
Omeprazole



Indirubin



C6-Methylenedioxybenzene

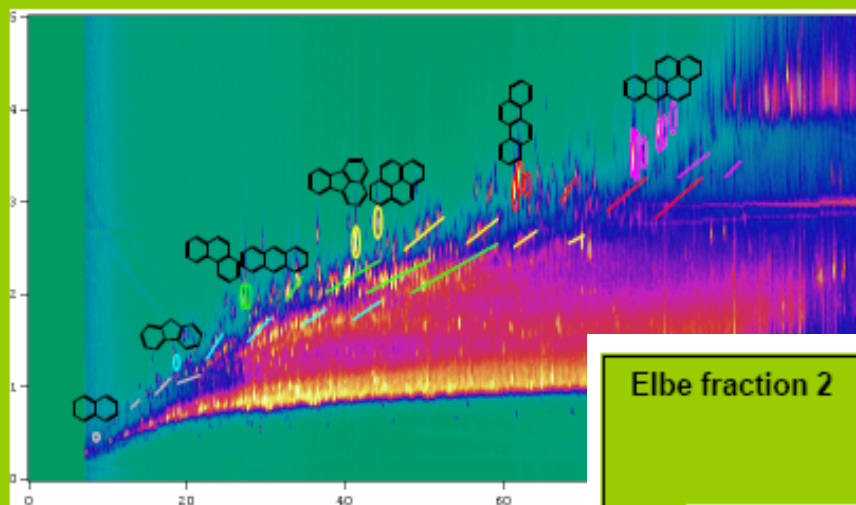


Tryptamine



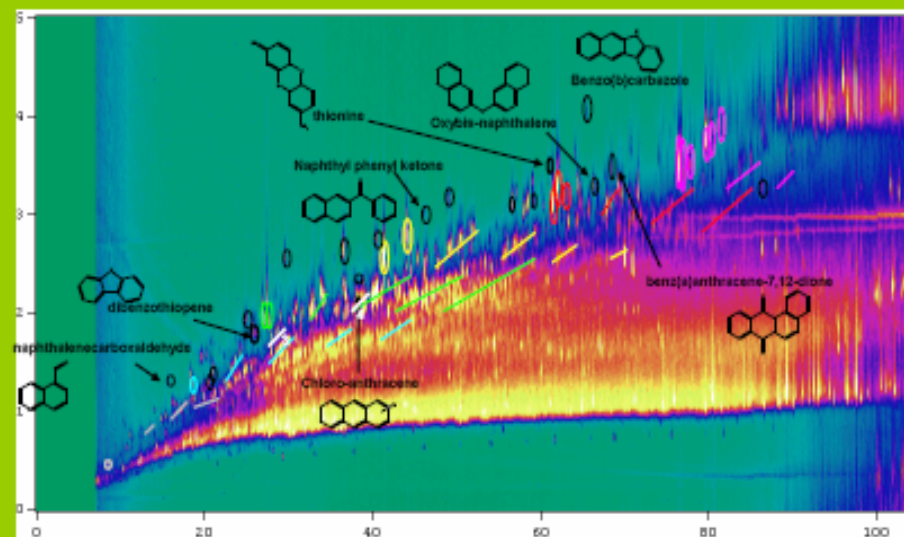
Elbe fraction 2

- Naphthalene
- Fluorene
- Phenanthrene and anthracene
- Fluoranthene and pyrene
- PAHs with MW = 228
- PAHs with MW = 252

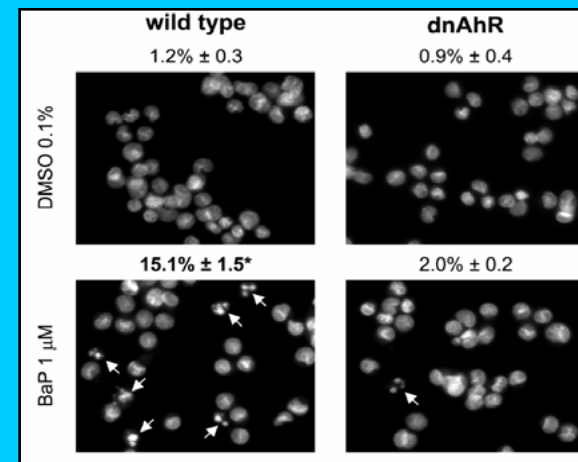
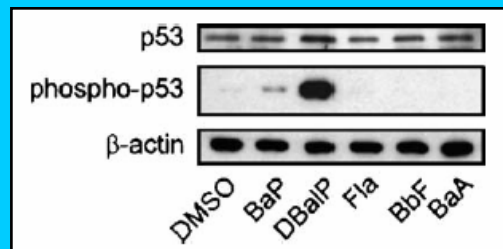
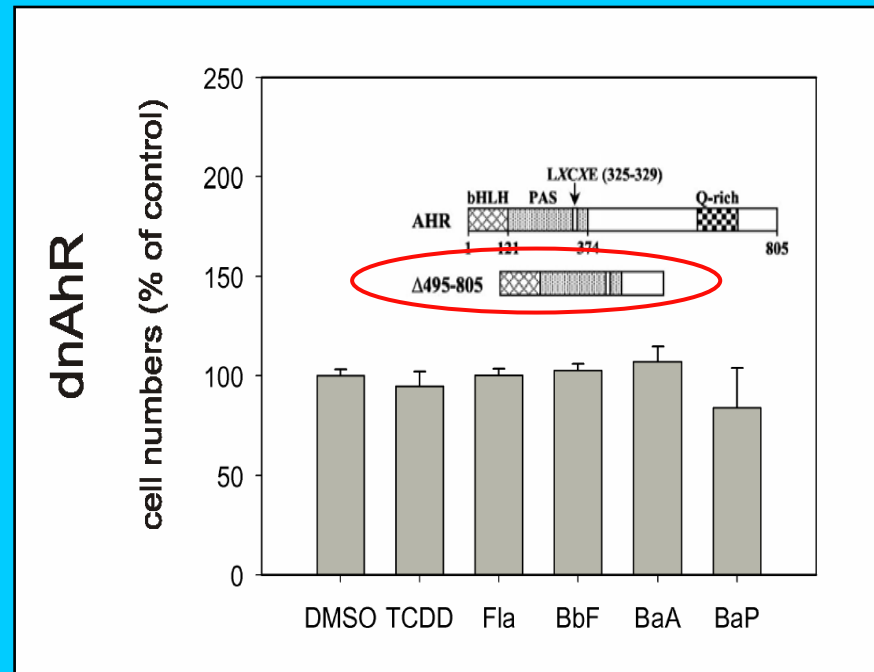
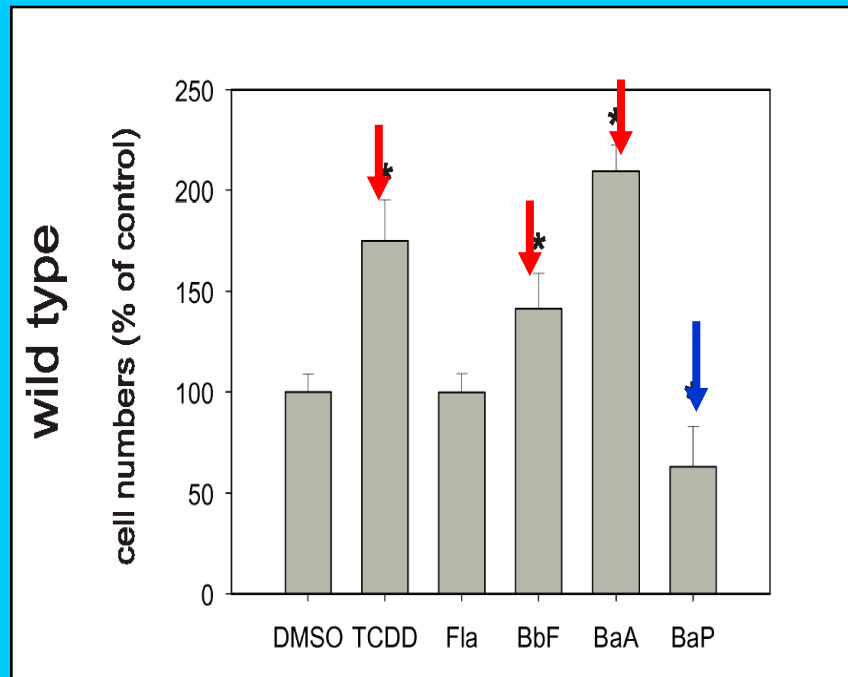


Elbe fraction 2

- Naphthalene
- Fluorene
- Phenanthrene and anthracene
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- PAHs with MW = 228
- PAHs with MW = 252

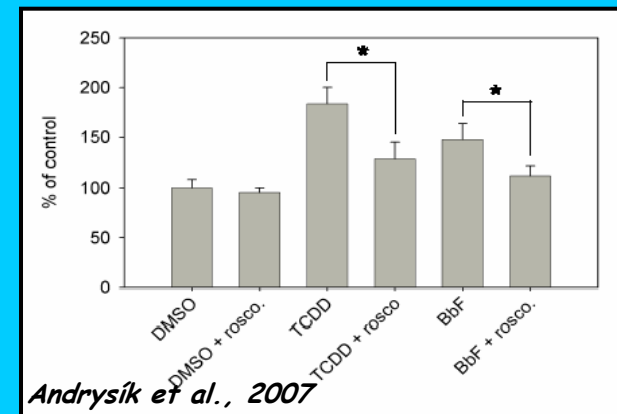
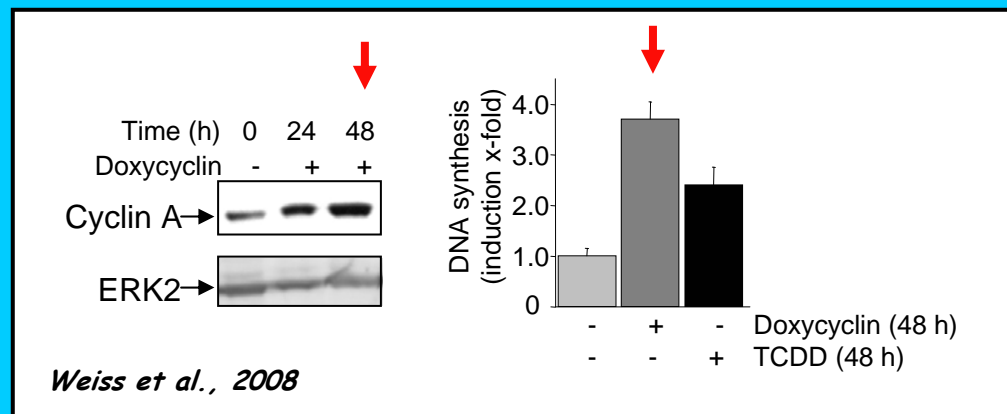
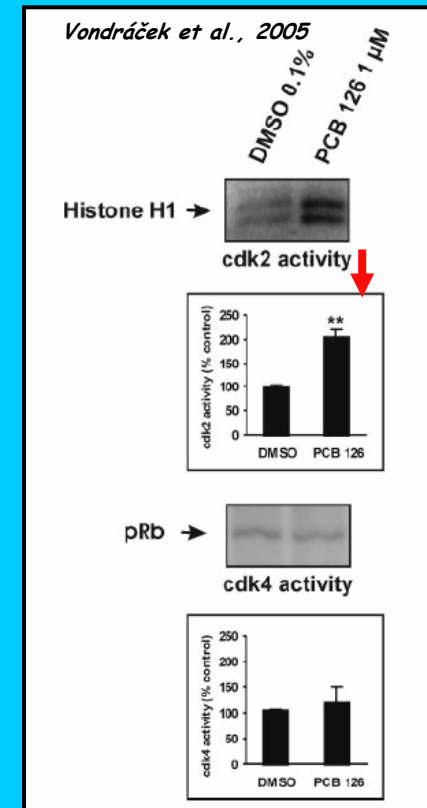
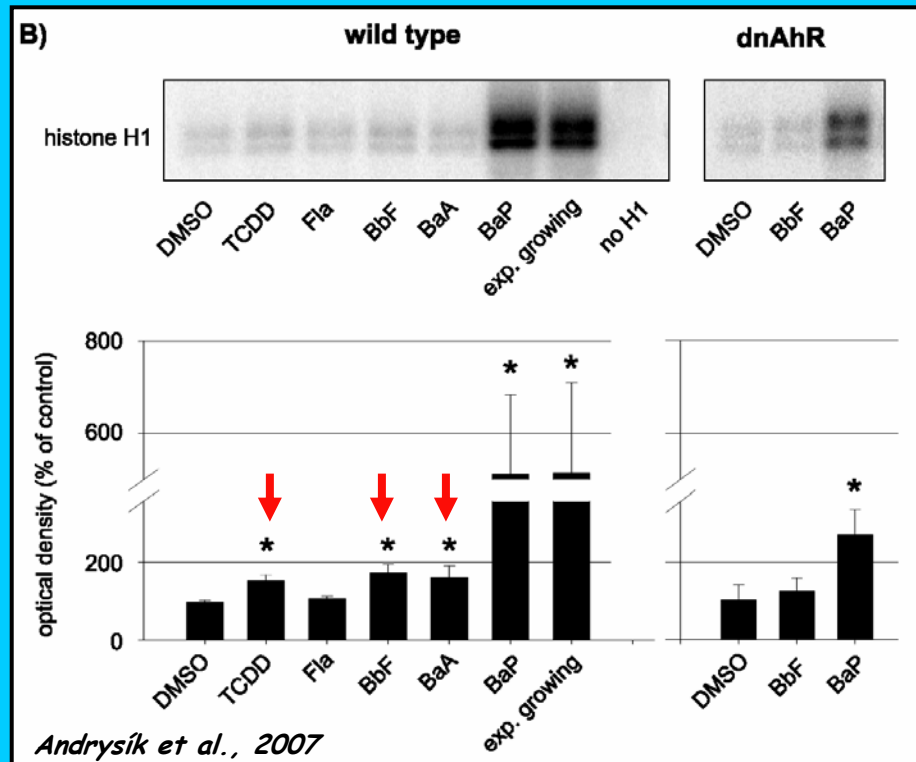


Expression of dnAhR blocks the proliferative effects of AhR ligands:

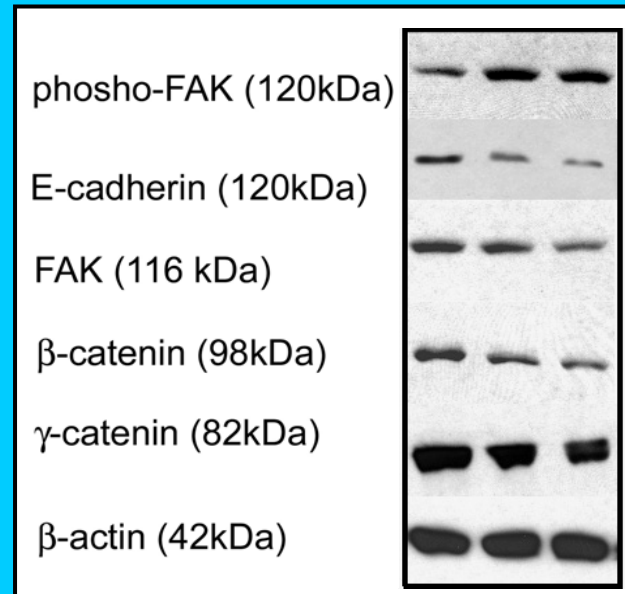
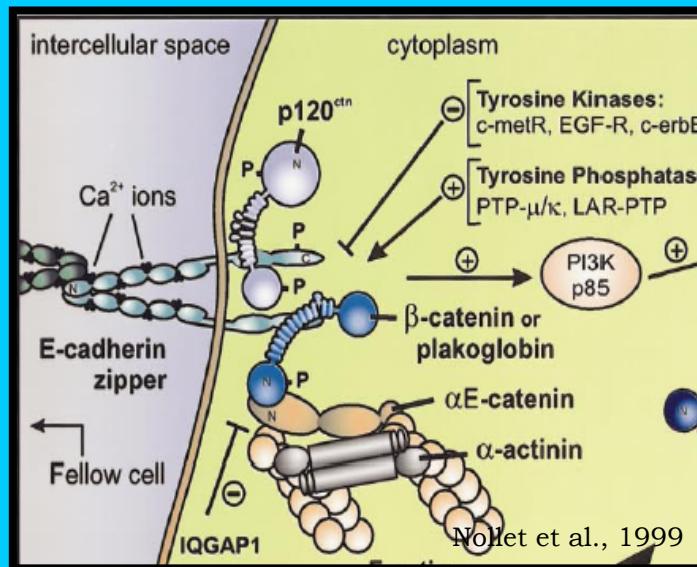


Andrysiak et al., 2006
Andrysiak et al., 2007

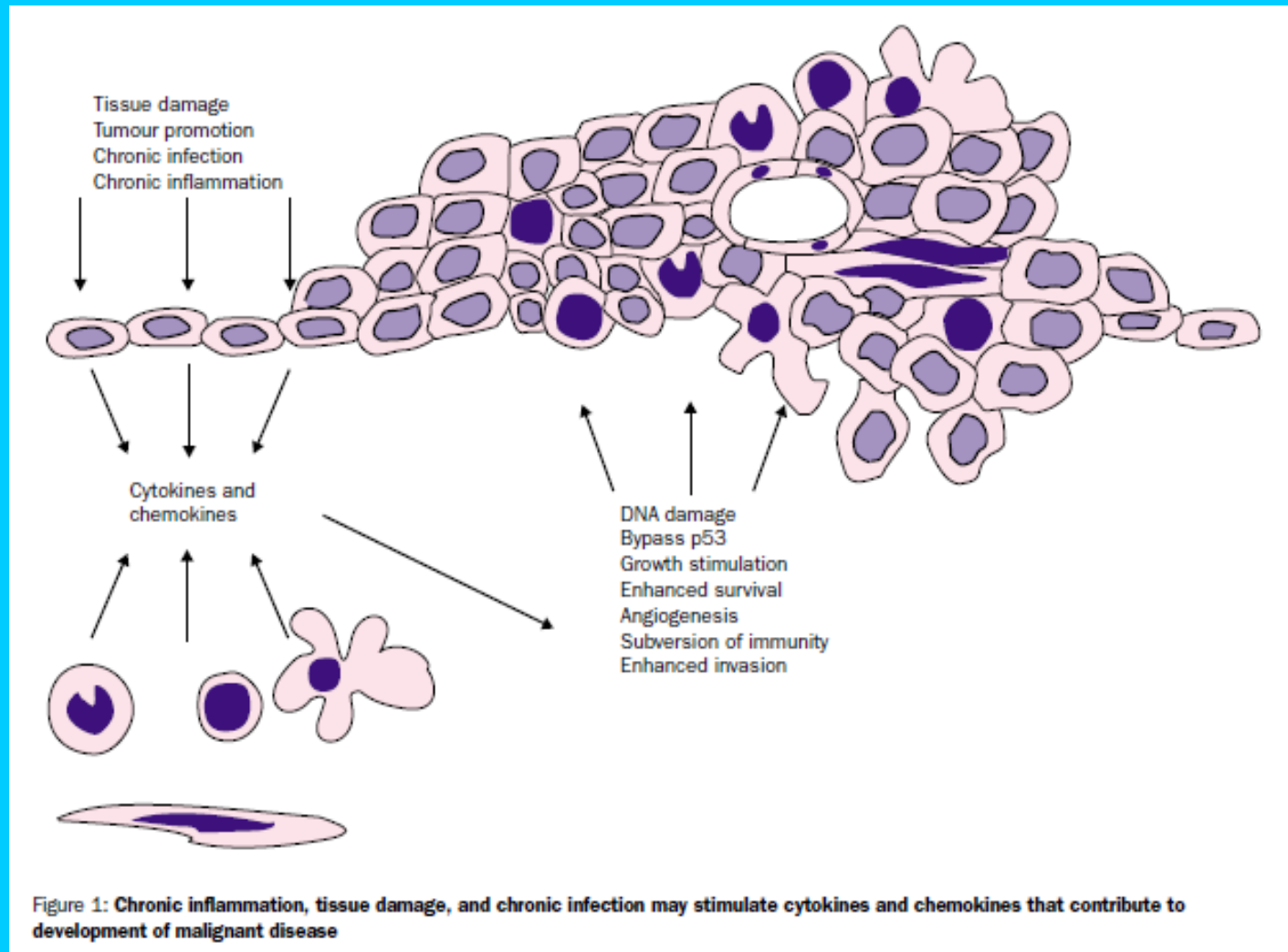
Cyclin A/cdk2 activity control is essential for the maintenance of contact inhibition:



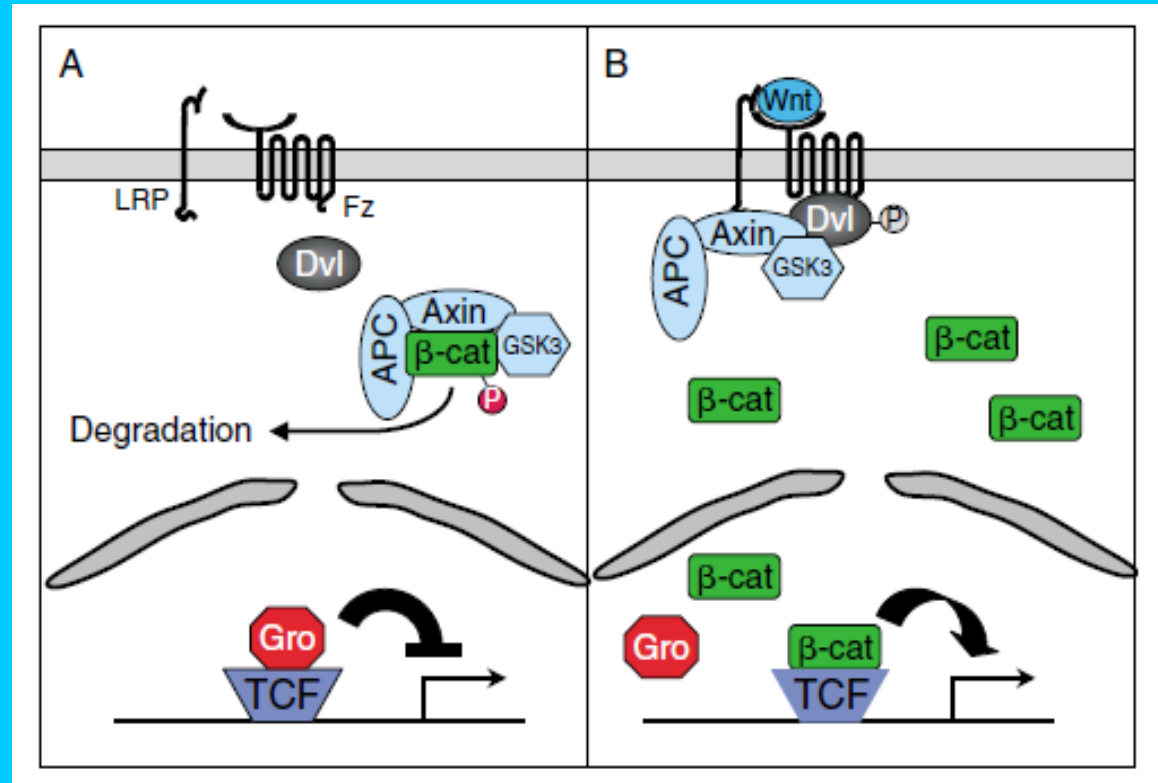
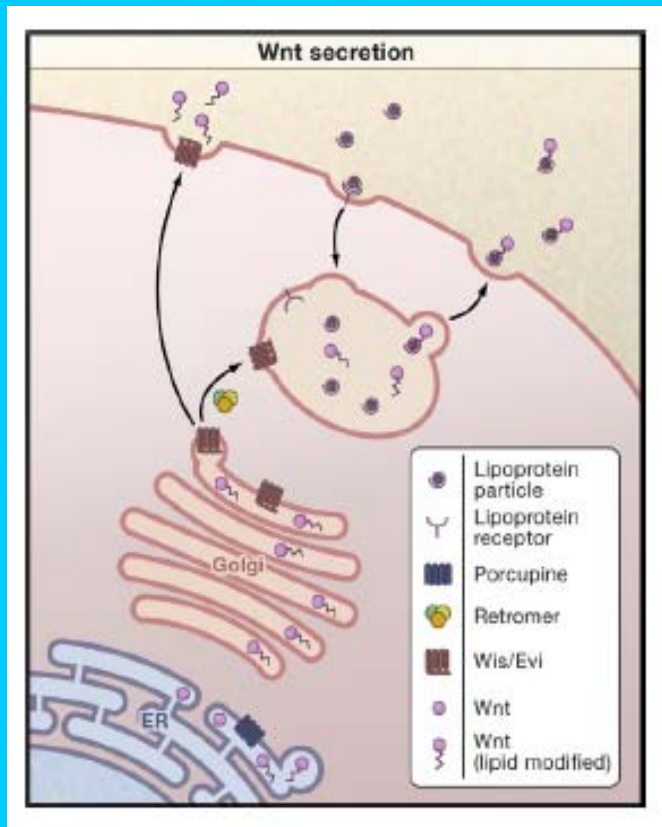
The story is more complex - AhR ligands disrupt also control of cell-to-cell communication - cell adhesion and gap junctional intercellular communication:



Interakce AhR a zánětlivých mediátorů v karcinogenezi



Interakce AhR a Wnt signalizace



Metodiky:

- kvantitativní real-time RT-PCR, Western blotting;
- průtoková cytometrie, fluorescenční mikroskopie;
- regulace genové exprese - EMSA, ChiP, expresní DNA mikroarraye;
- manipulace genové exprese - siRNA, transientní a stabilní transfekce buněk;
- in vitro buněčné kultury, in vivo pokusy, práce s klinickým materiálem;
- in vitro testy toxicity