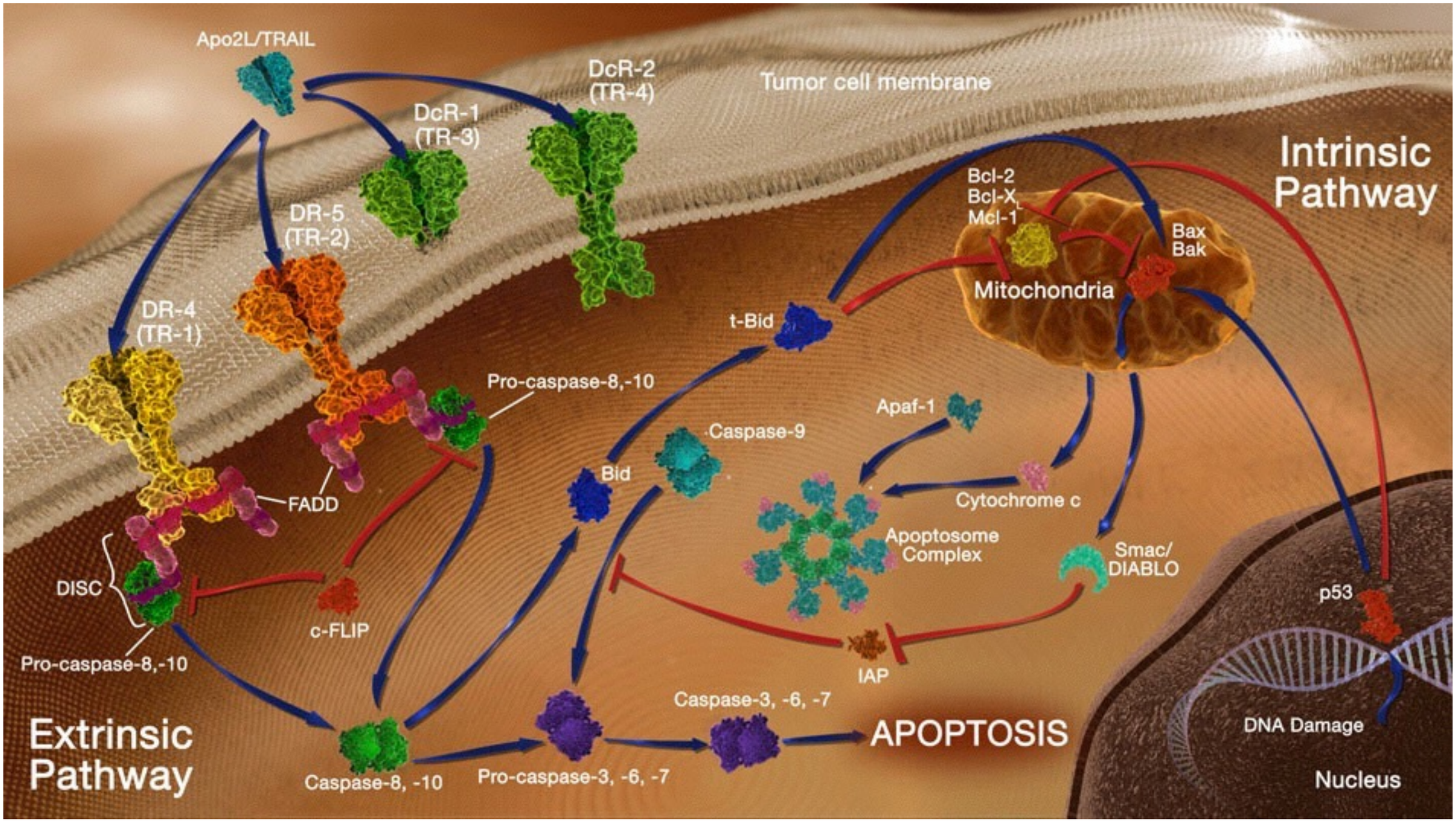
Gene expression profile of cell lines with acquired TRAIL resistance, multicellular TRAIL resistance and sensitivity

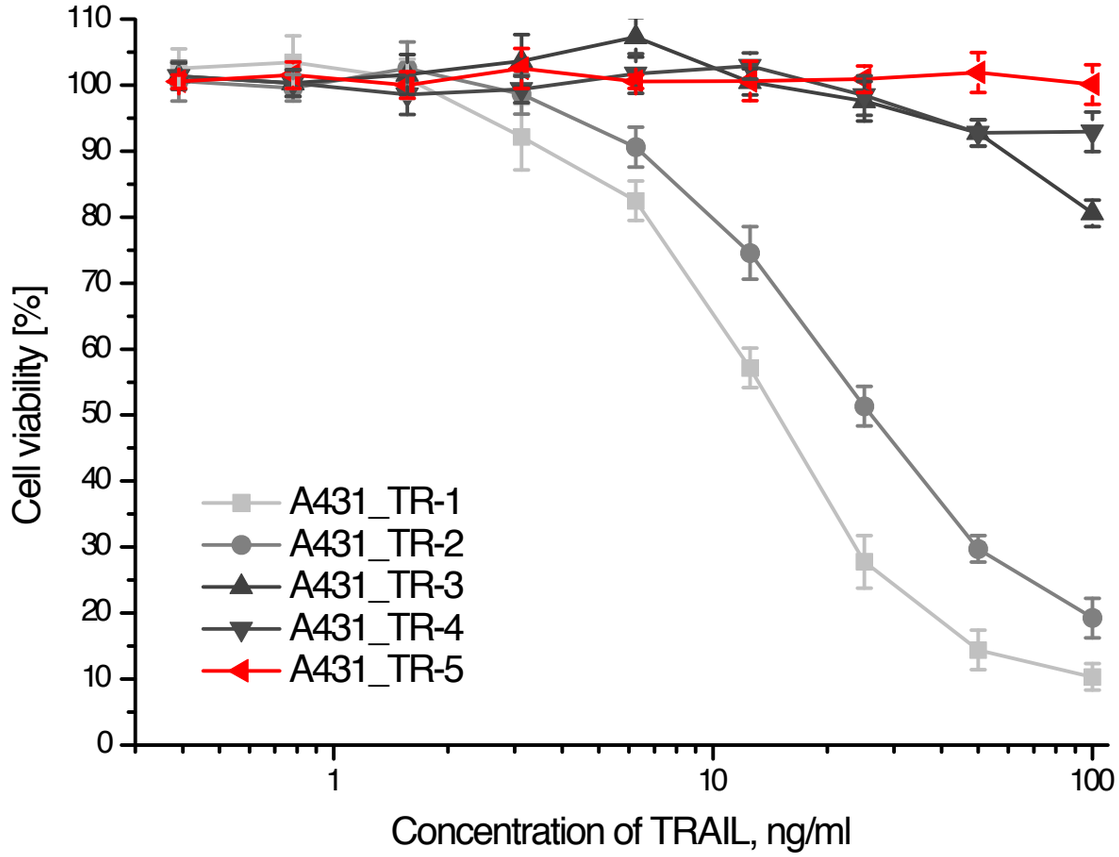
Nadezda Dolgikh

The TRAIL kills cancer cells



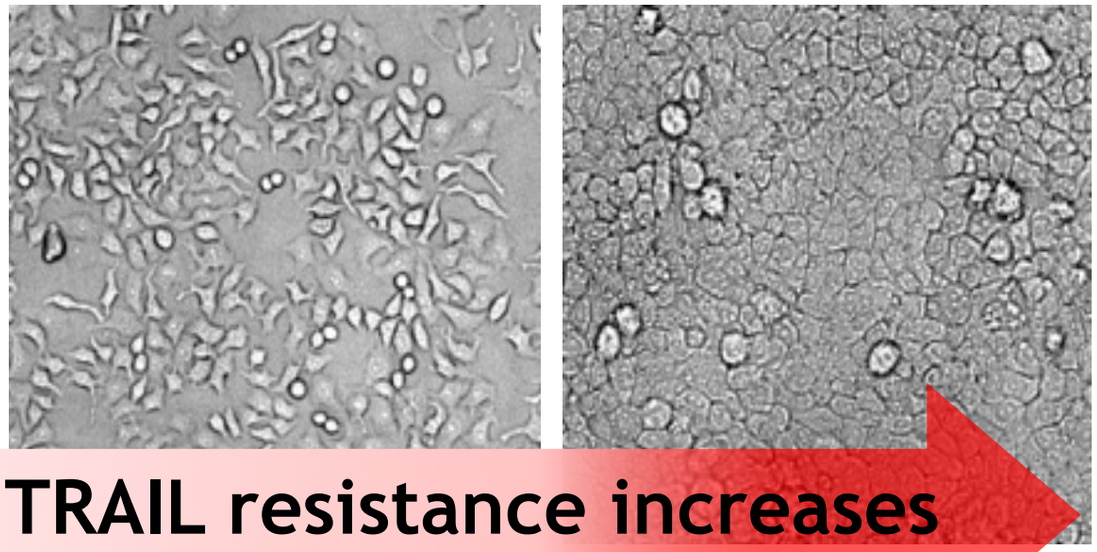
http://www.amgenoncology-international.com/#/our-products/our-pipeline/

Types of Resistance:
Acquired TRAIL-resistance

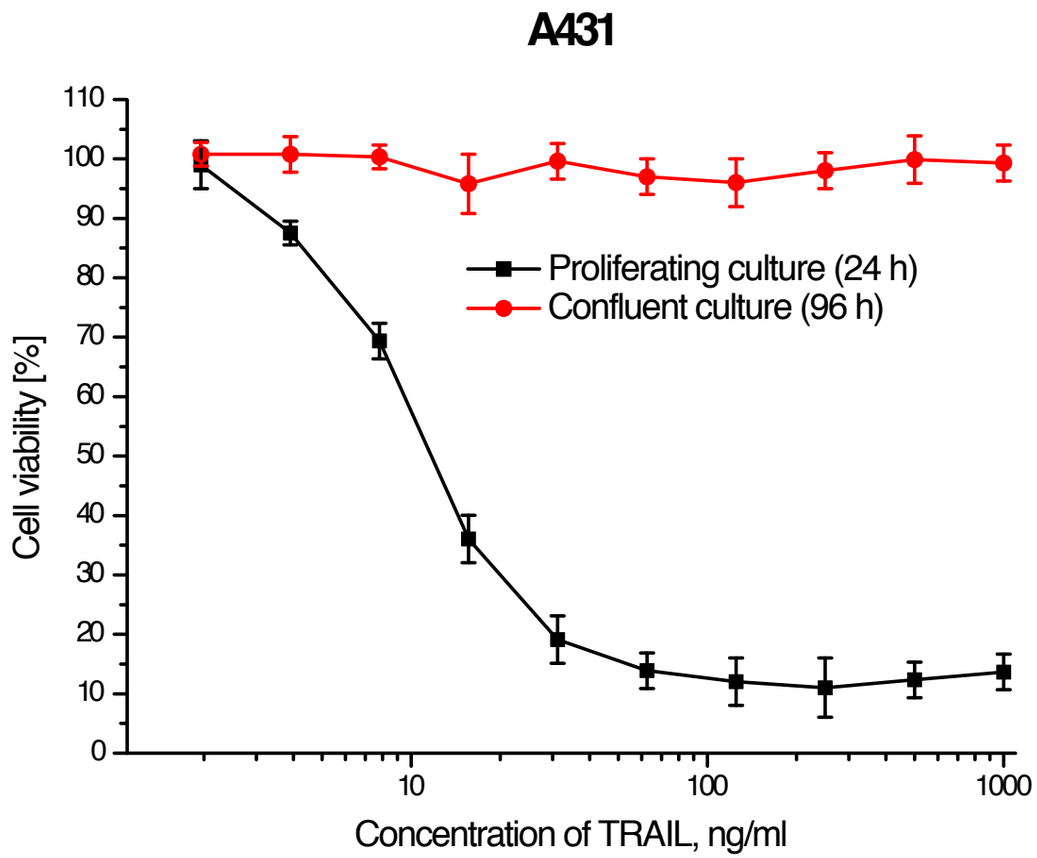


Types of Resistance:
Multicellular TRAIL-resistance

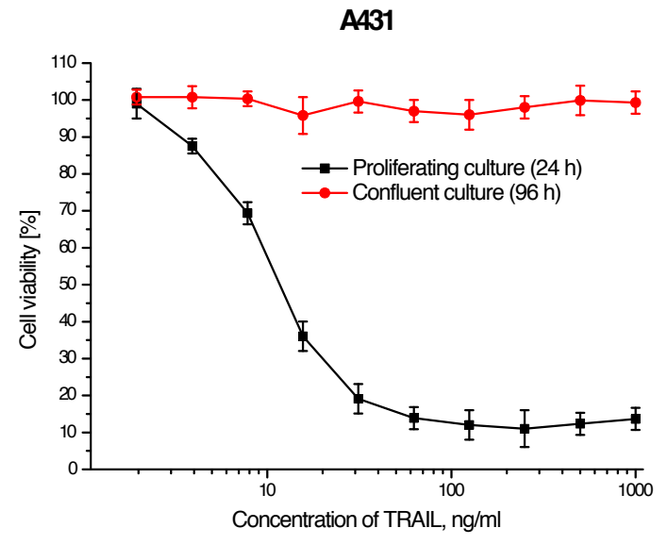
Proliferating culture **Confluent culture**



TRAIL resistance increases

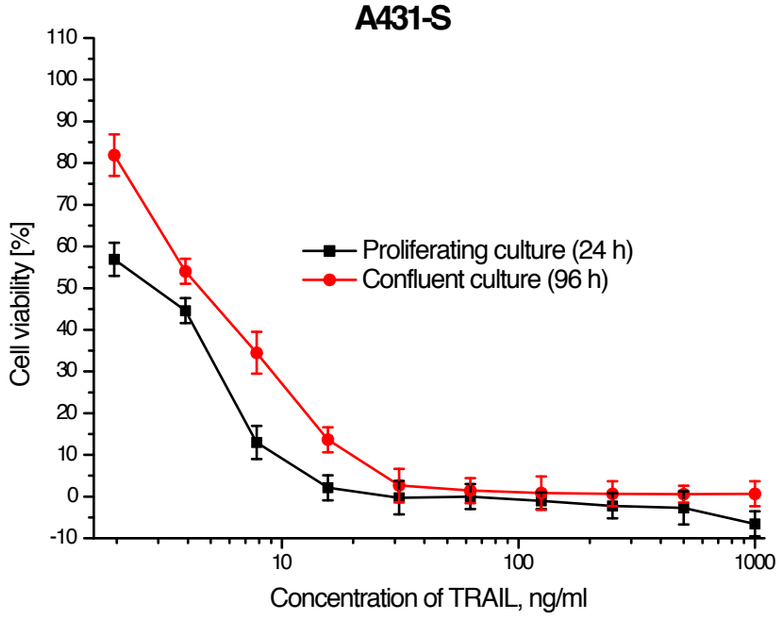


We obtain sub-cell lines with different types of TRAL-sensitivity/resistance

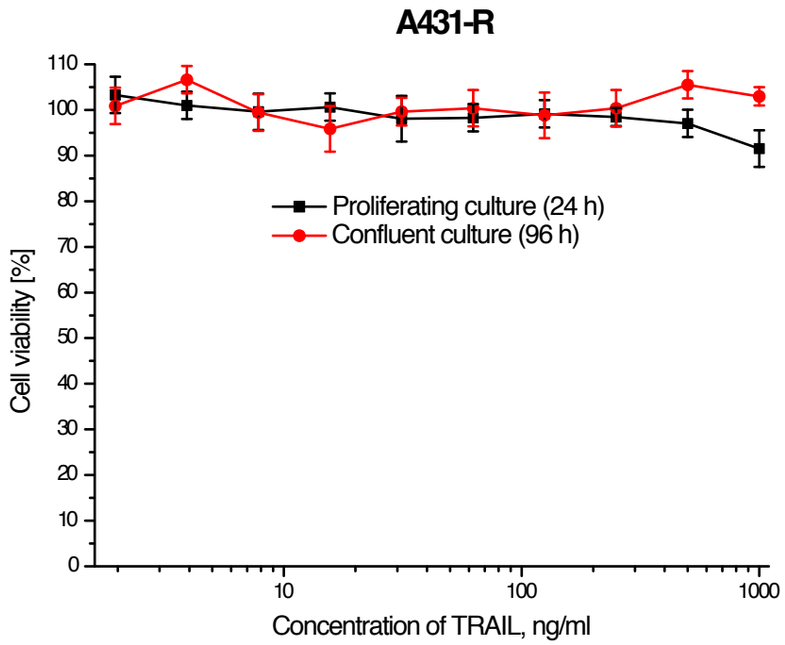


Parental A431 cell line:

- TRAIL-sensitive in proliferating culture
- TRAIL-resistant in confluent culture



TRAIL-sensitive cells in confluent



TRAIL-resistant cells in proliferating culture

Results of Gene expression profile

Molecular mechanism of multicellular resistance:

- Parental A431 multicellular vs. proliferating condition
- Parental multicellular vs. A431-S multicellular condition

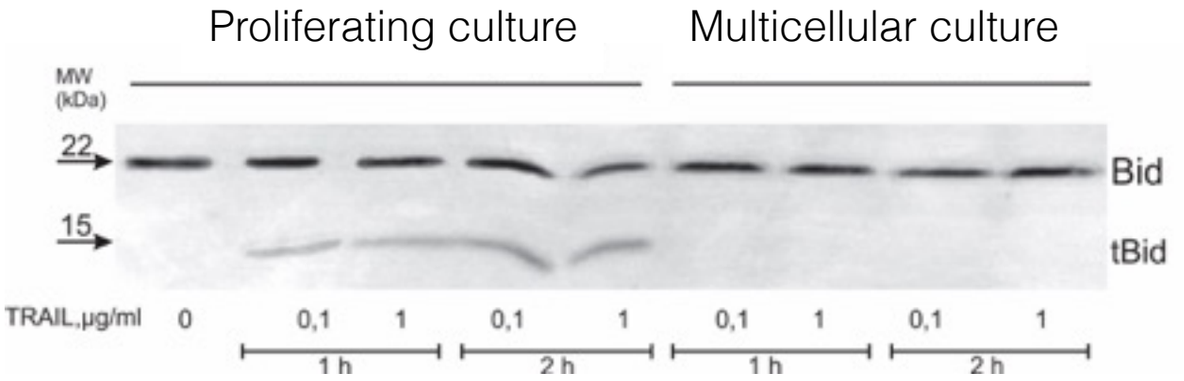
Molecular mechanism of acquired resistance:

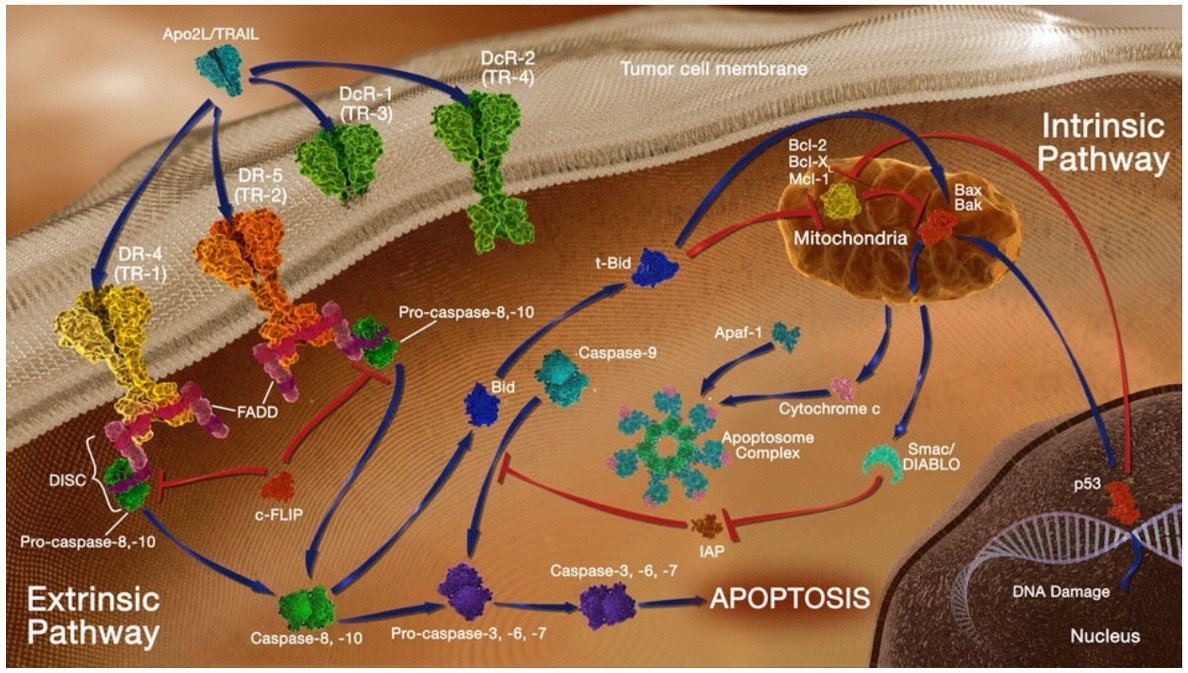
- A431-R proliferating vs. Parental A431 proliferating conditions

In TRAIL-resistant cells:

- Down-regulated pro-apoptotic genes (BH3-only proteins)
- Up-regulated anti-apoptotic and pro survival genes (Bcl-2, Mcl-1, CD68, CDK6, ISG15, cFLIP and so on)

Validation of results





In Multicellular TRAIL-resistant cells Bid cleavage does not occur

↓

Disruption of the signal transduction form ligand-receptor complex to mitochondria