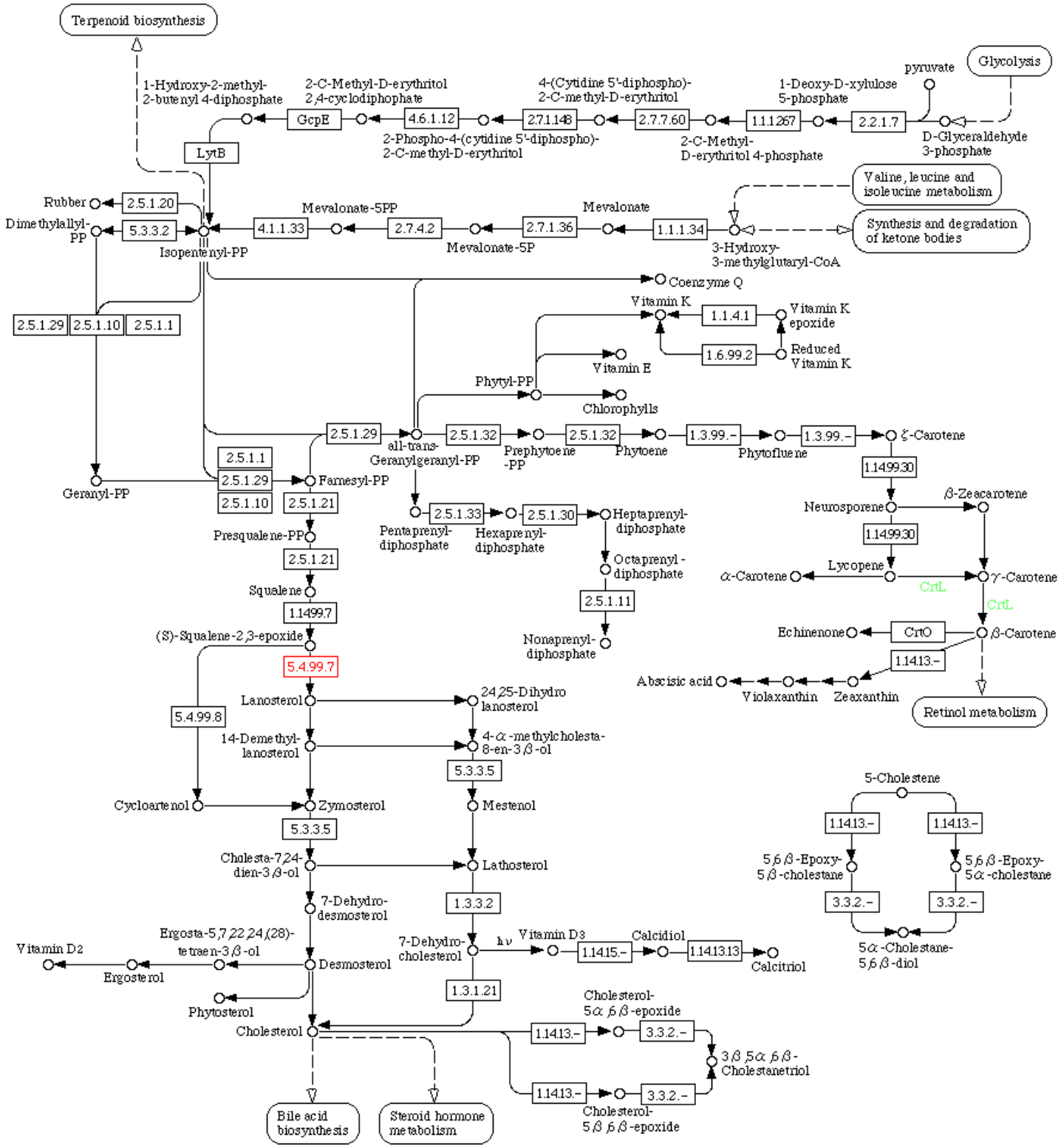
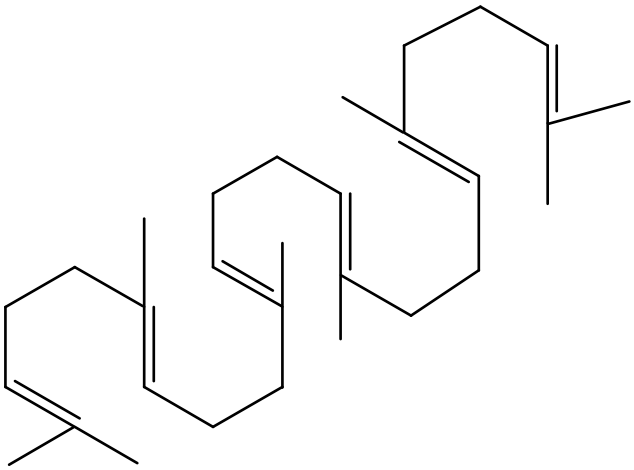
I. Exemplár

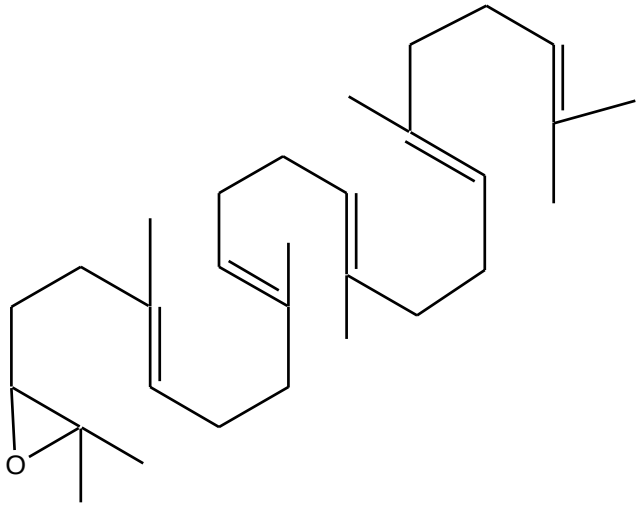
Biológiailag érdekes 3 eset, amit soha nem tanítottam még

STEROL, VITAMIN K, VITAMIN E, CAROTENOIDS BIOSYNTHESIS



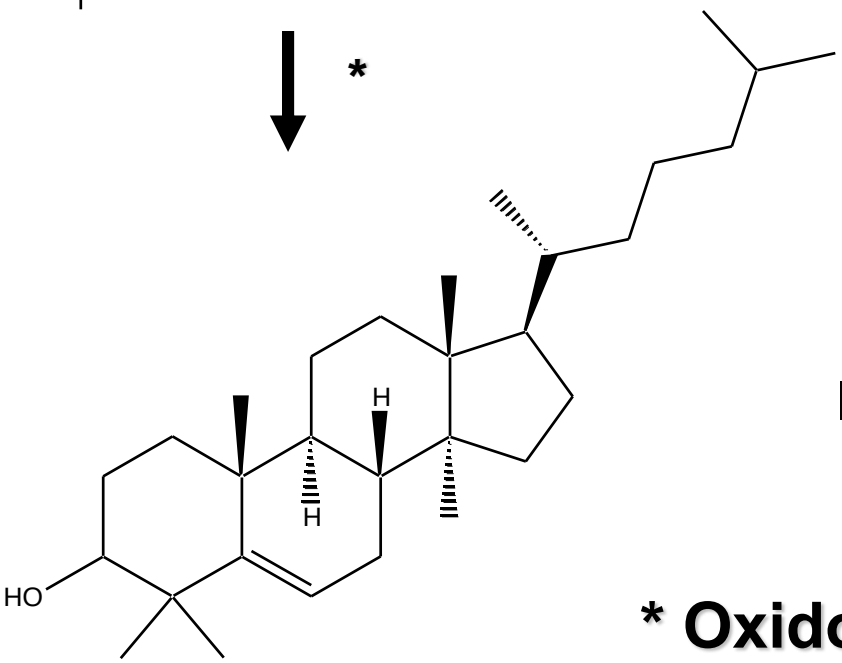


szkvalén



(S)-2,3-epoxid-szkvalén

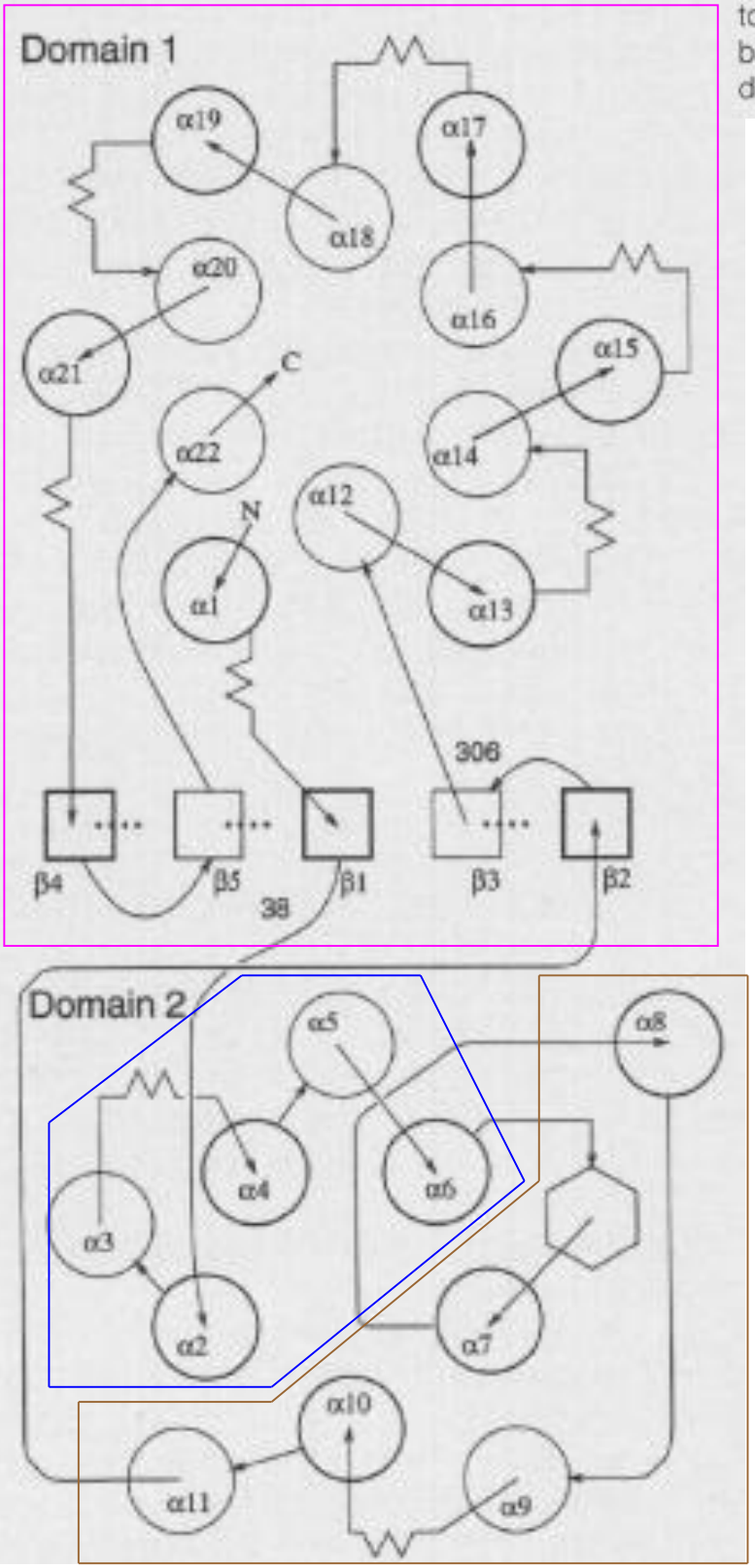
*



lanoszterol

*** Oxidoszkvalén cikláz**

Fig. 3. Chain fold topology showing α helices (circles), one 3_{10}-helix (hexagon), β strands (squares), and QW-motifs (zigzag) with marked chain directions upward (thin) and downward (thick). Domain border positions are given. The top sketch shows how the outer ring of the α_6-α_6 barrel is stabilized by the QW-motifs, one of which deviates from the others.



Domain 1 Hélixei:

Belső:

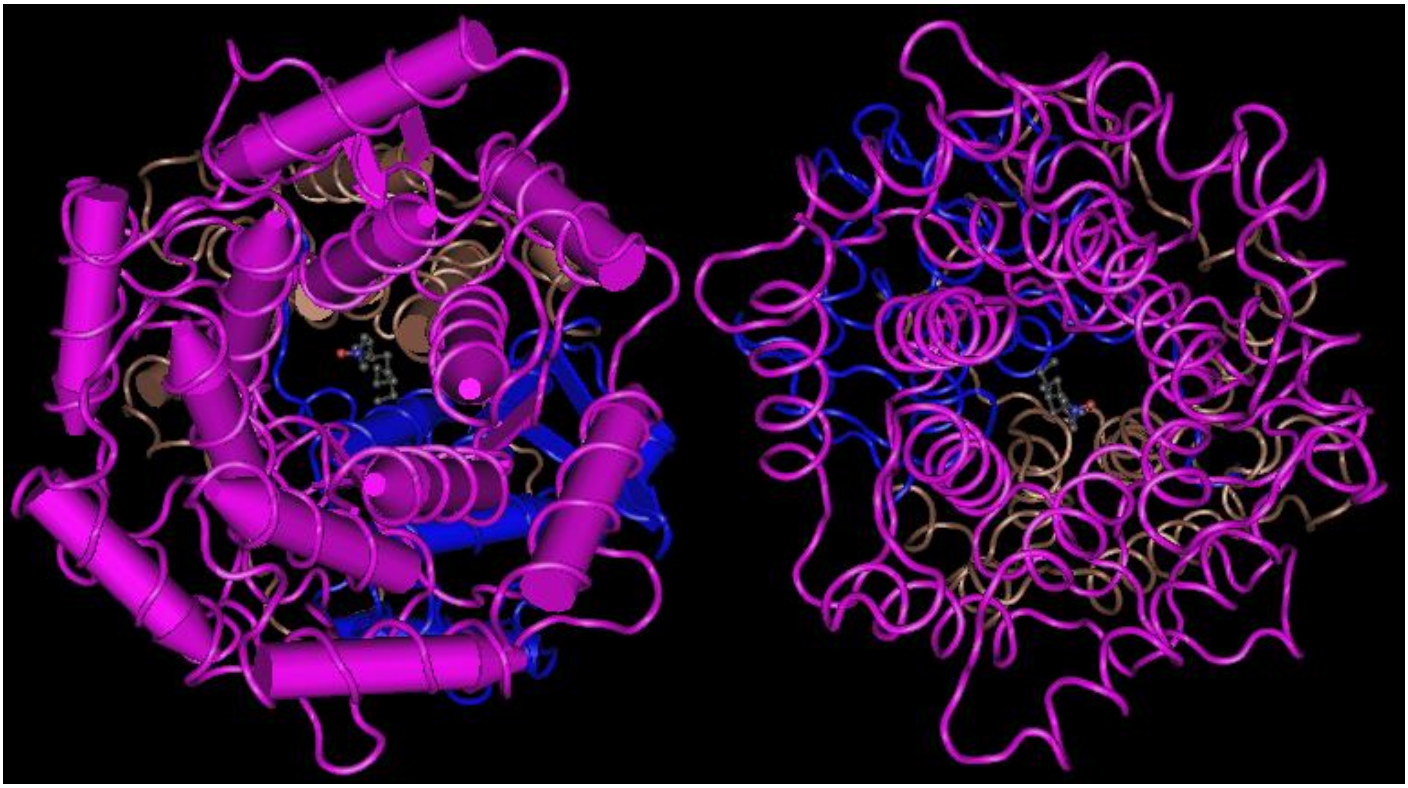
PVWDTGLAVLALRAA
VDDTAVVVWALNT
EDVTAHVLECFGSF
NYLYGTGAVVSALKAV
PSQTAWALMALIAG
YRHVFPTLALGRYKQ

Külső:

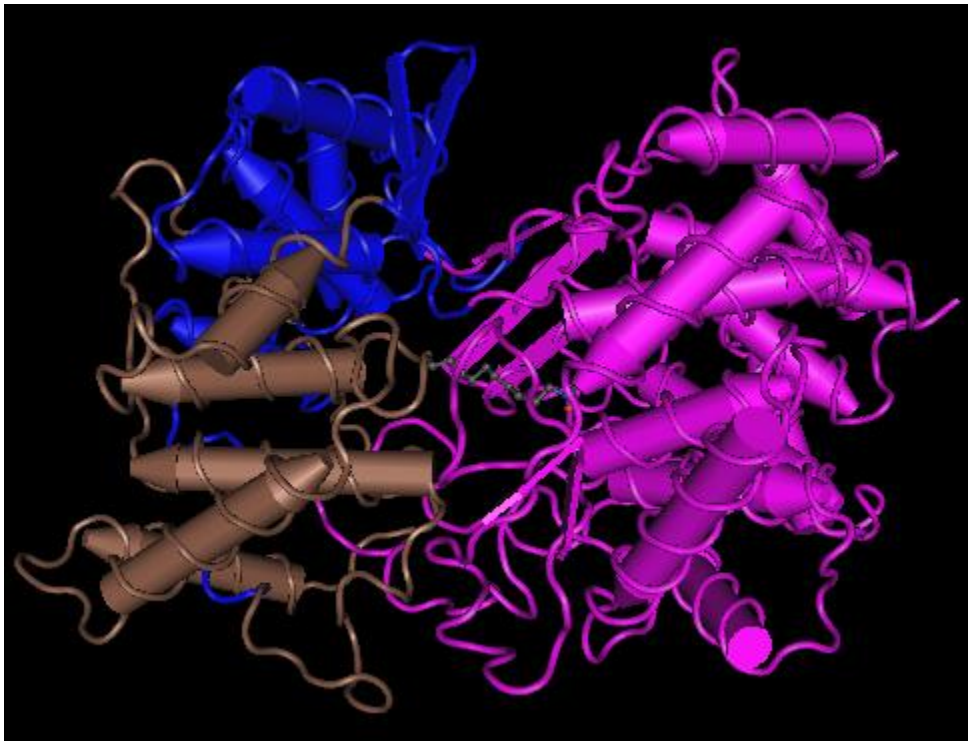
YARTLDRAVEYLLSC
DRLVKAGEWLLDR
ERRRRDAMTKGFRWIVGM
KVIRRAVEYLKRE
PYIQKALDWVEQ
EAARRGVQYLVET

DE: savas
RK: bázikus
IVT: β-elágazó
WYFH: aromás

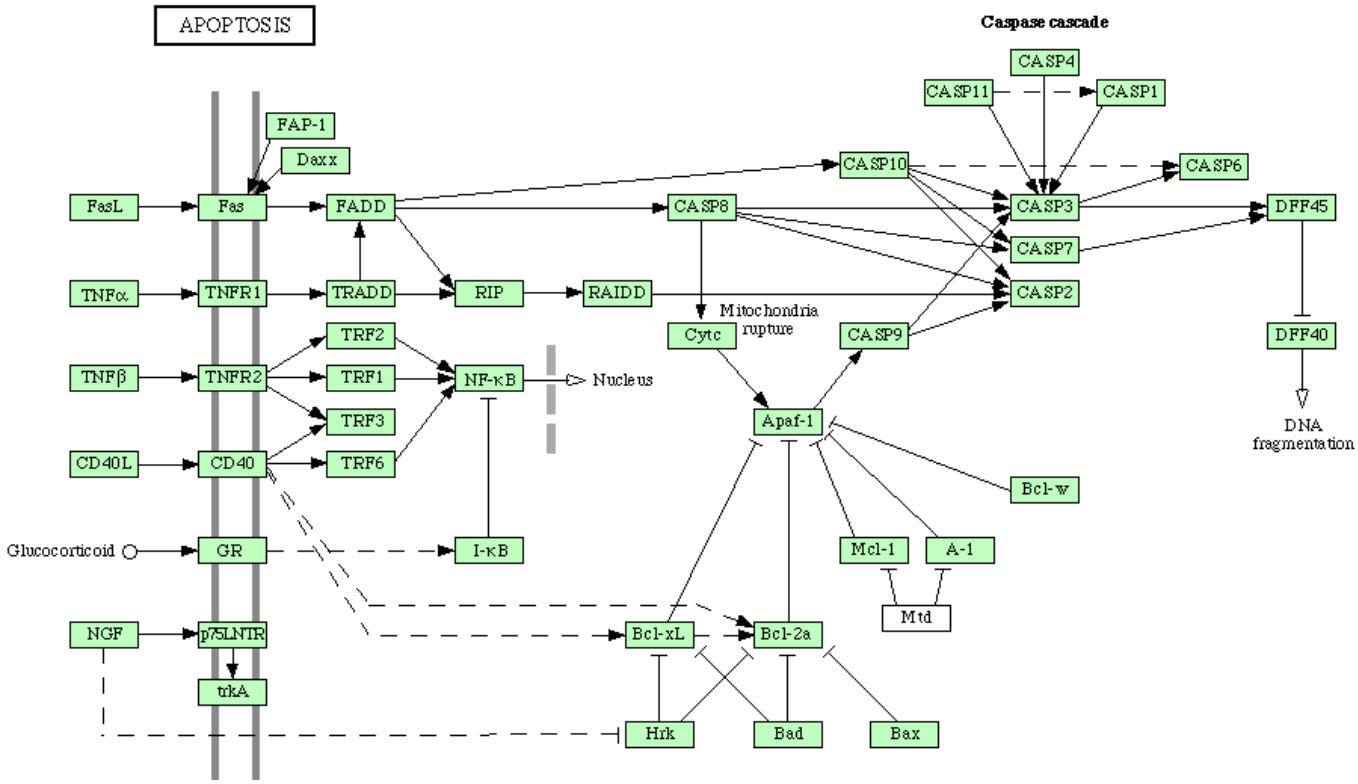
Science, **1997**, 277:1811-15



Szkvalén cikláz PDB: 1SQC
(*Alicyclobacillus acidocaldarius*)



II. Exemplár



One theory about the molecular basis of HD-induced vesication proposes the following sequence: HD alkylation of purines in DNA leads to activation of the nuclear enzyme PARP; and PARP activation rapidly depletes NAD^+ with consecutive impairment of glycolysis and ATP production.[1] However, other investigators described only poor correlation between the maintenance of NAD^+ levels and cell death.[4] Nevertheless, HD concentrations of $\geqslant 500\ \mu M$ significantly depleted ATP in keratinocytes 5 h after HD injury.[6] In contrast, in our experiments SCL II showed no significant ATP depletion during the first 6 h after HD injury. However, 12 h later a loss of ATP at HD concentrations of $\geqslant 500\ \mu M$ was observed. Possibly SCL II cells have a more potent defense system (e.g. glutathione) than keratinocytes.

Recently Rosenthal *et al.* reported evidence that HD induces apoptosis and terminal differentiation (programmed cell death) in keratinocytes.[11] Intracellular ATP levels have been described recently as a 'switch' between apoptotic and necrotic cell death. After induction of apoptosis, ATP-dependent steps were identified up- and downstream of caspase 3.[22,25] Therefore, damaged cells seem to need a certain level of ATP for progression towards apoptosis.[26,27] Accordingly, the maintenance of normal ATP levels in SCL II cells for several hours after cell injury might be an important signal triggering apoptotic death. Our data showed a clear concentration- and time-dependent increase in apoptotic SCL II cells after HD injury. In contrast, the fraction of necrotic cells showed only a slight time- and dose-dependent increase. An HD concentration of $\leqslant 10\ \mu M$ only slightly affected SCL II viability in short-term assays. However, cell proliferation showed a progressive loss of cells 120 h after HD injury. These cells also showed typical fragmentation of the nucleus, indicating apoptotic death. Low concentrations of HD ($<1\ \mu M$) also reduced the colony-forming ability of SCL II cells. Therefore, we conclude that HD induced not only early apoptotic death in SCL II cells but also late apoptotic death, as deduced from the observed 'reproductive death' in the colony-forming assay.

Smith *et al.* observed a cell cycle arrest of keratinocytes in the late G1/early S phase after HD injury,[28] which indicates an increase in DNA repair mechanisms. In this context, PARP activation is one of the first steps observed. Keratinocytes exposed to 100 μM HD show a PARP activation only after 2 h and PARP is not cleaved into the characteristic 89-kDa and 24-kDa fragments at this concentration within 24 h.[11] Additionally, no NAD^+ and ATP depletion in keratinocytes was observed at 5 h after 250 μM HD. It seems reasonable that activation of DNA repair at low concentrations of HD does not lead merely to growth arrest. Insufficient DNA repair after several hours and days might induce late apoptotic death in keratinocytes in a similar manner as in SCL II cells.

Sejthalál

Intracelluláris ATP szint:

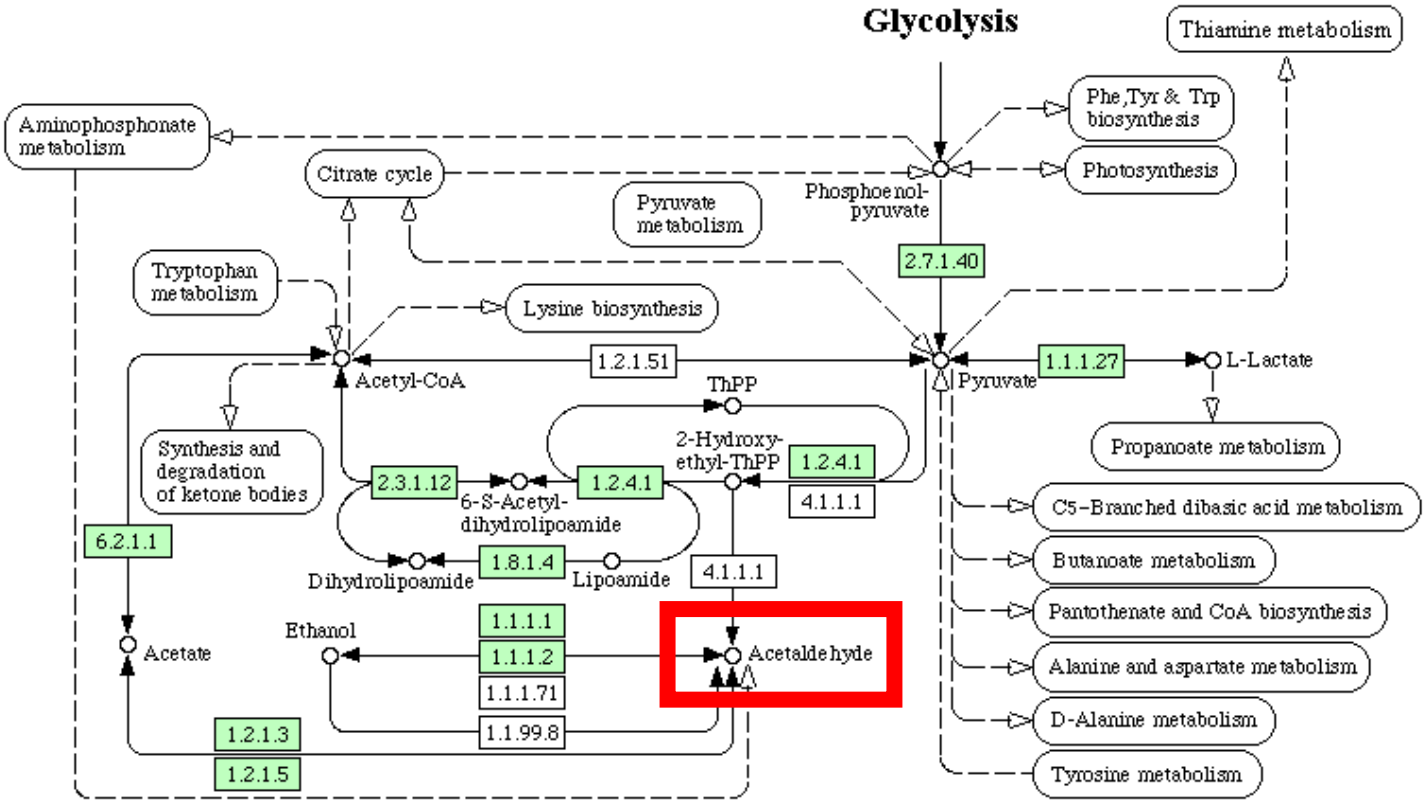
Alacsony→ **nekrózis**	Magas→**apoptózis**
A sejt és vezikulumai felduzzadnak	A sejt zsugorodik A kromatin kondenzálódik és a magmembrán szélén helyezkedik el

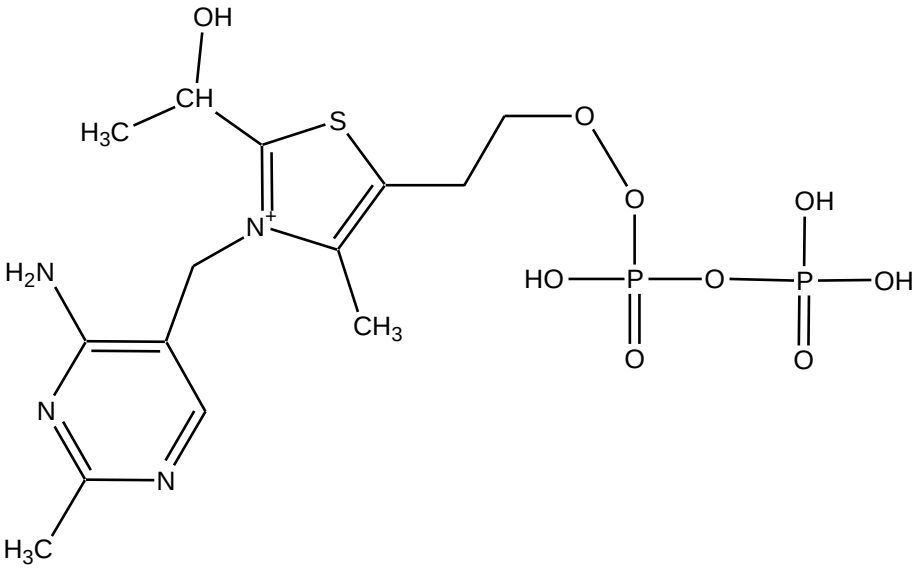
Caspase 3 központi szerepe az apoptózisban: Cisztein proteáz, mely proteolitikus hasítás révén aktiválódik. Továbbá katalitikusan aktív tiol-csoportja nitrozilálódik, ekkor inaktív az enzim. Denitrozilálódással újra aktiválható az enzim.

FAS és TNFR jelátviteli szerep. Ezekhez Death Domain tartalmú fehérjék kapcsolódnak: FADD és TRADD.
FADD +/+ normál genotípus: caspase 3 aktiválódás,
FADD -/- genotípus: caspase 3 nem aktiválódik.
Kénmustár hatására apoptózis illetve nincs apoptózis.
A caspase 3 végső soron (többek között) aktiválja a CAD-t (caspase associated DNase) és a DNS-javító poli (ADP-ribóz) polimerázt (PARP).

J Biol Chem, **2003**, 278 (10): 8531-8540

III. Exemplár





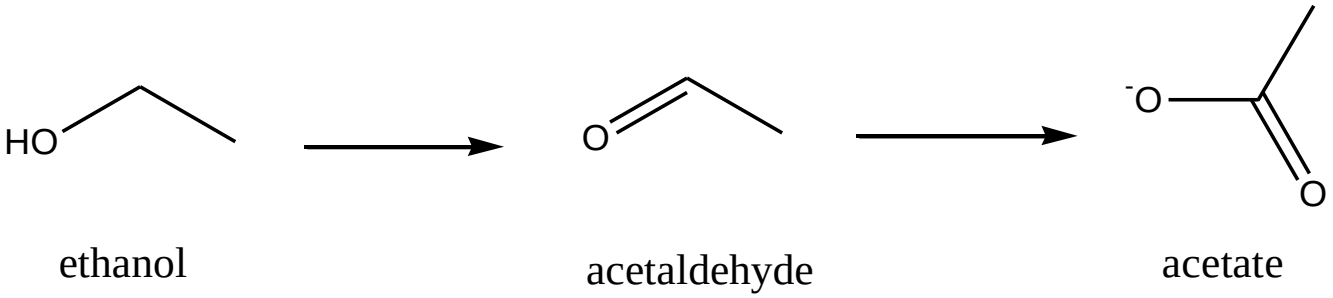
2-(α-hidroxietil)tiamin difoszfát
2-hidroxietil-ThPP

Napi alkoholfogyasztás:

20-30g Csökkenti a kardiovaszkuláris megbetegedések okozta halálesetek számát. Ezáltal növeli az élettartamot.

60g férfiaknál, nőknél 40g naponta viszont már növeli különböző betegségek kialakulásának a valószínűségét.

J Clin Pathol. 1983 36(4):365-78



Kollagén I és III szintézis növekszik (fibroblaszt ill májsejt) hepatic fibrogenezis.

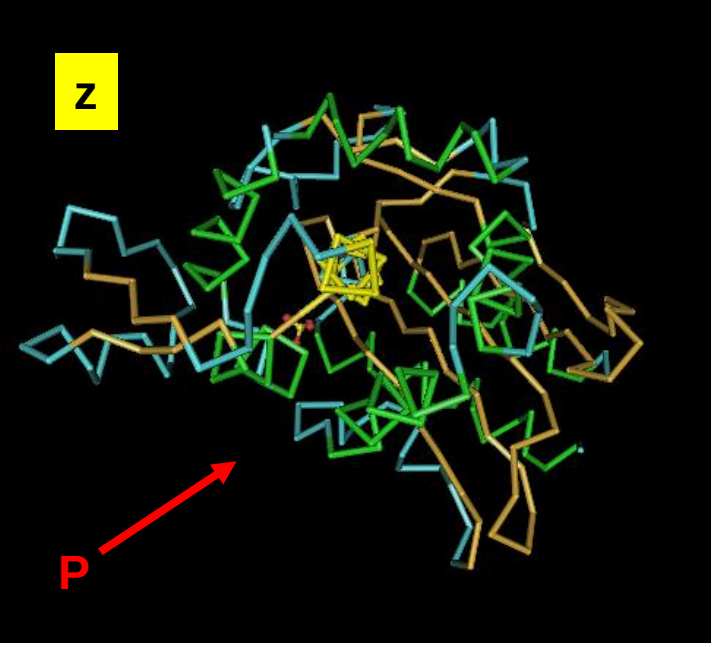
Brenner J Biol Chem. 1987 262(36):17690-5

Alcohol Clin Exp Res. 1999 23(2):279-84

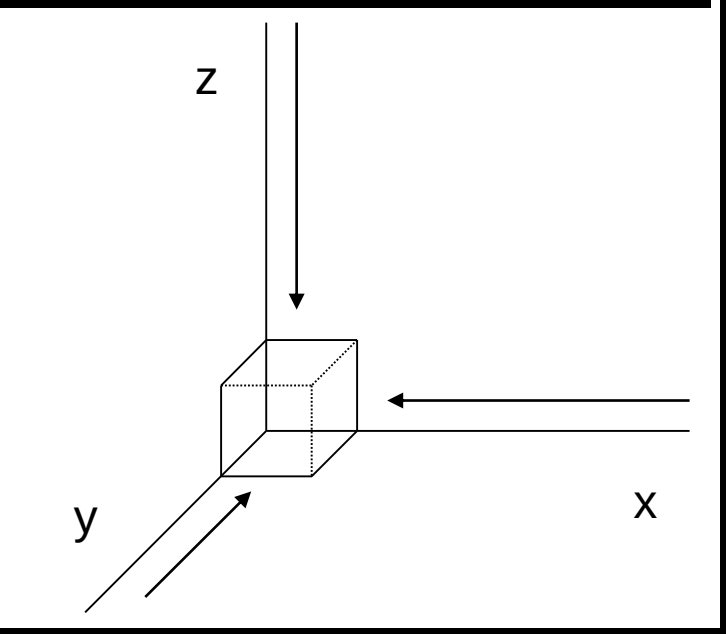
Chen Mol Cell Biol. 2000 20 (8): 2818–2826

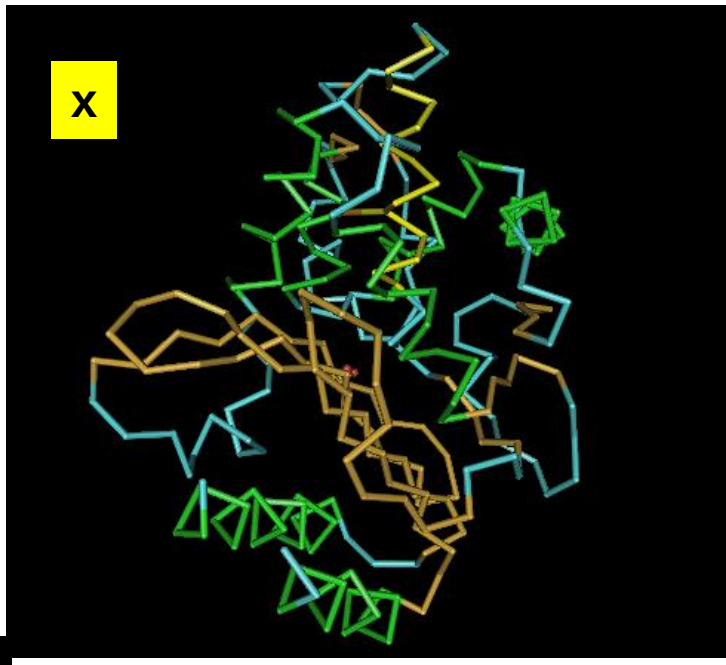
Biochem. J. (2002) 368: 683–693

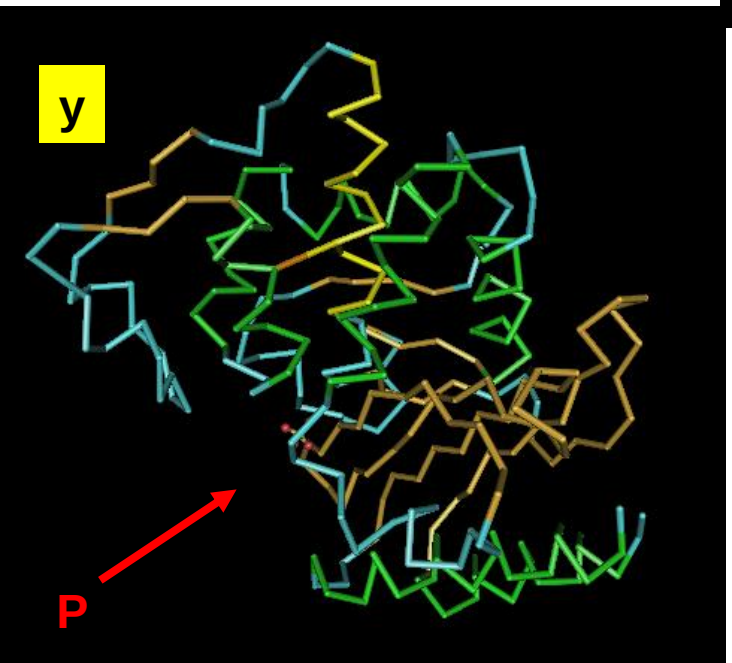
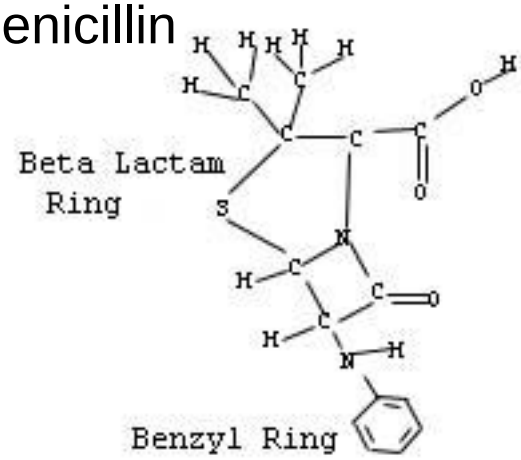
IV. Exemplár



Penicillináz vagy β-laktamáz







P: penicillin