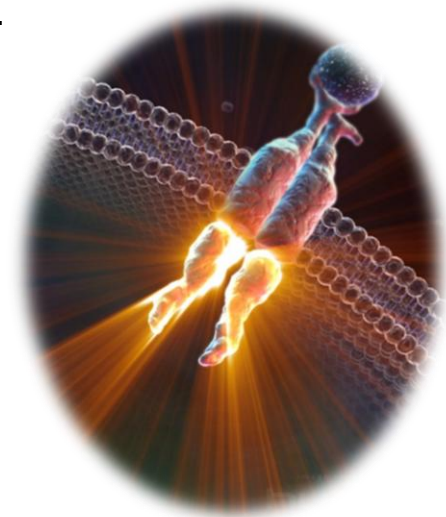
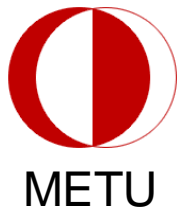


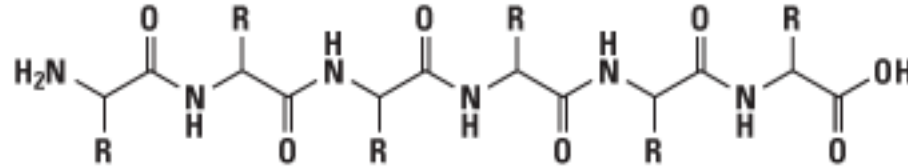
Peptide Drug Discovery and Design

Can Ozen

SYBORG (Synthetic Biology Research Group)
ProVenom Ltd. Co.
Central Laboratory
Center of Excellence in Biomaterials and Tissue Engineering (BIOMATEN)
Biotechnology Department



Peptides



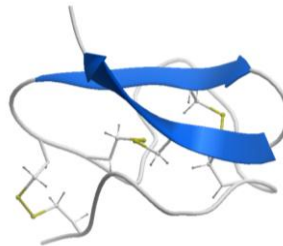
- Short Proteins (2-100 aa)
- 20 genetically encoded amino acids + non-standard aa
- A simple 10 aa peptide: **10 Trillion Combinations !**

Protein Folding Problem

DCGHLHDPCPND
RPGHRTCCIG
LQCRYGKCLVRVGR
[Sequence]



U1-TRTX-Sp1a
[Structure]



Neurotoxin
[Function]

- Range of biological activities is truly remarkable !
- Hormones, cytokines, neurotransmitters, toxins, antibiotics

Peptide Drugs



- ~ 60 marketed peptide drugs (Frost & Sullivan 2014)
- ~ 270 in clinical phase
- ~ 400 in advanced preclinical phase

Advantages

- Small (Higher tumor penetration)
- Ease of synthesis and modification
- Diversity
- More potent
- High specificity (minimized side effects)
- Low toxicity
- No organ accumulation
- No drug-drug interactions

Disadvantages

- Size
- Cost of production
- Stability (Fast clearance)
- Membrane transport
- Oral bioavailability



Venom Peptides



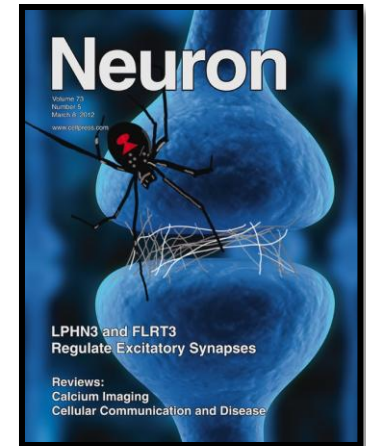
- 100,000 species of venomous animals
 - Snakes
 - **Scorpions**
 - **Spiders**
 - Sea Anemones
 - Insects
 - Worms



**"Poison is in everything and no thing is without poison.
The dosage makes it either a poison or a remedy."
Paracelsus (1493-1541)**

- Enzymes, **peptides**, polyamines, neurotransmitters, amino acids, nucleotides, ions
- 38000 spider species / ~500 peptides from each venom
- **~20 Million bioactive peptides !**
- Only ~1000 identified so far

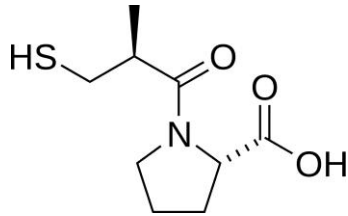
- Most venomous peptides target ion channels and receptors
- **Around 70% of the drugs targets are ion channels and receptors**



Peptide Drugs From Venom

Captopril

- 1981
- Snake
- Hypertension
- Annual Sales > \$1B



Integrilin

- 1998
- Snake
- Antiplatelet



Prialt

- 2004
- Cone snail
- Painkiller



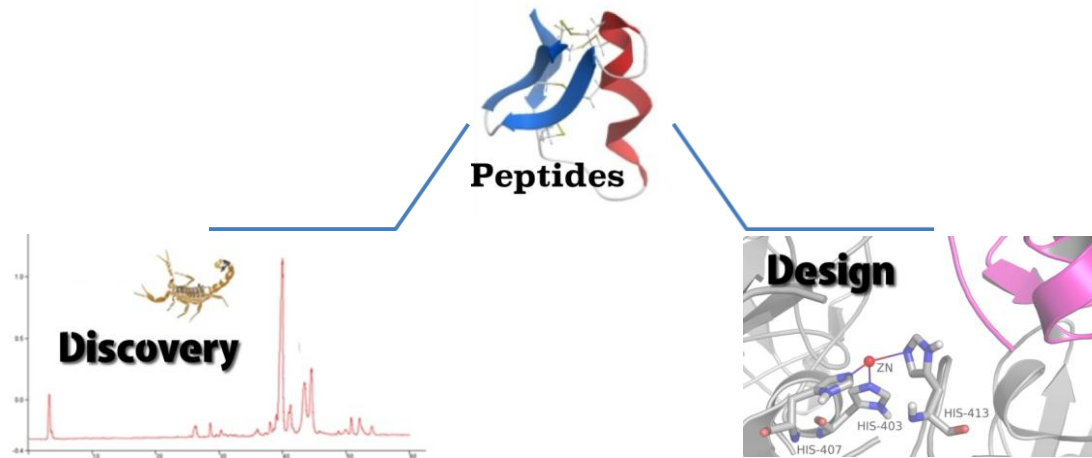
Byetta

- 2013
- Gila monster lizard saliva
- Type II diabetes



- 2010: Founded
- Located at Central Laboratory
- Member of Center of Excellence in Biomaterials and Tissue Engineering [BIOMATEN]
- 2013: Focused on discovery and design of therapeutic peptides
- 2014: Spin-off company, ProVenom Ltd. Co., launched

Discovery and Design of Therapeutic Peptides



Animal Venoms
Peptidomics / Transcriptomics
Cell-based Assays (Screening)

Venom Peptides
Structural Biology
Peptide Engineering

Peptide Drug Discovery

Specimen Collection
Farming
Venom Milking



Kadir Boğaç Kunt



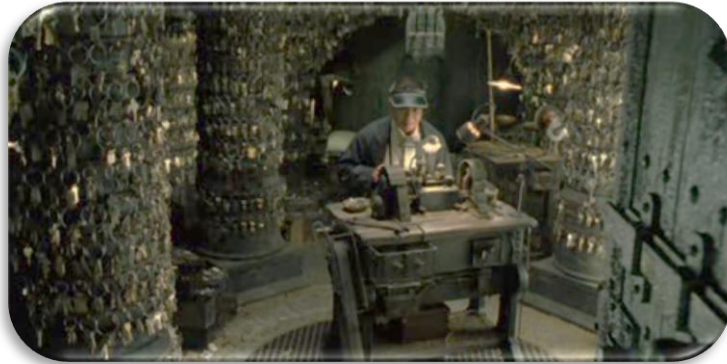
Titus tunnel (Hatay)



Arachnid specimens

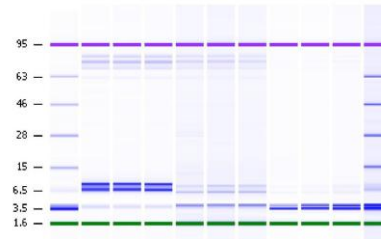


Peptide Drug Discovery

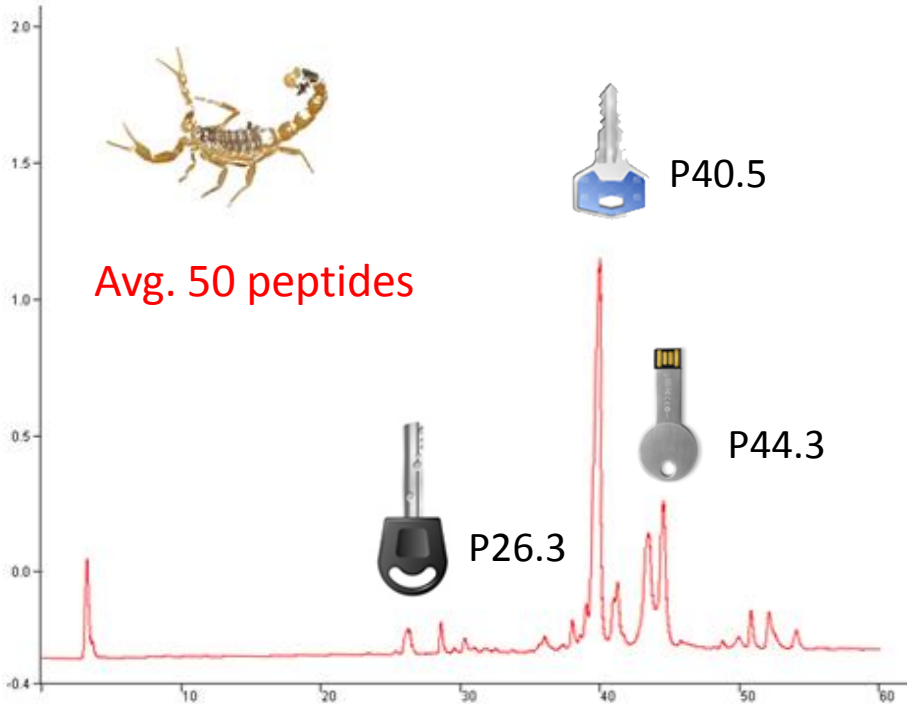


The keymaker (Matrix Reloaded, WB)

Peptidomics Transcriptomics



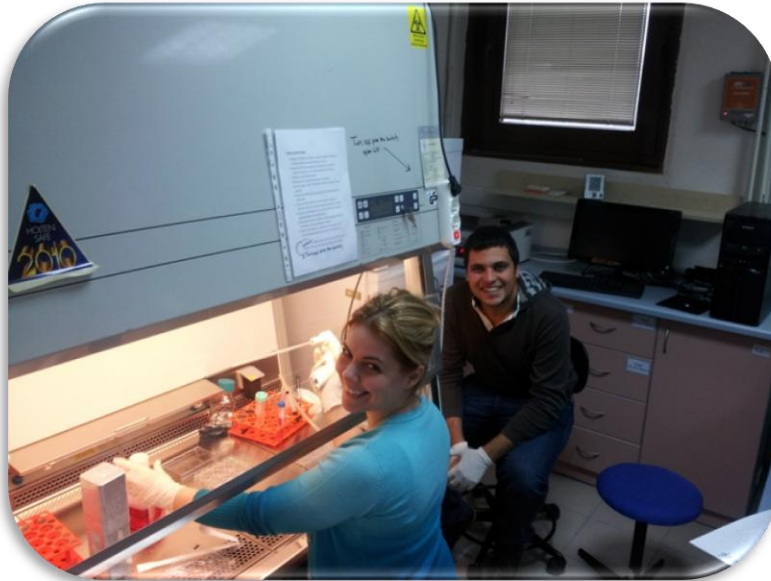
Electrophoretic profile of a Scorpion crude venom



Prostar Varian HPLC (MERLAB)



Peptide Drug Discovery



ipek and Efe conducting a cytotoxicity assay on cancer cells.

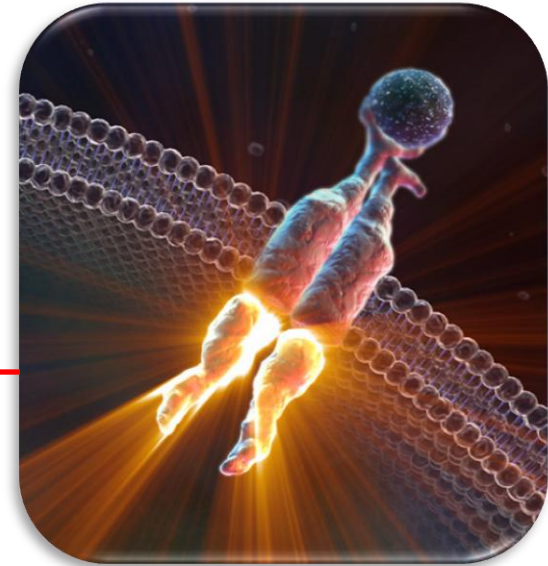
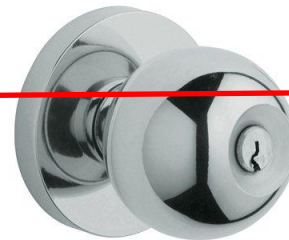
Cell-based Assays [Screening]



Peptides [Keys]



Receptors [Locks]

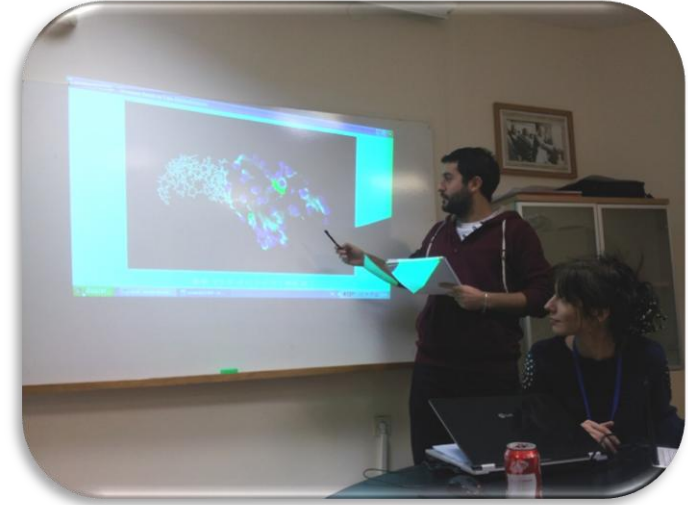
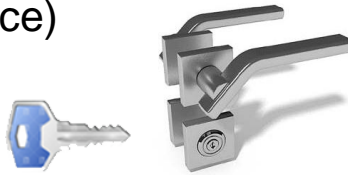


Activated receptor
[Hybrid Medical Animation]

Peptide Drug Design



- Cloning / Expression / Purification
- Peptide Synthesis
- Molecular Modeling / Docking
- SPR (Surface Plasmon Resonance)
- ITC (Isothermal Titration Calorimetry)
- Enzyme Kinetics
- NMR (Nuclear Magnetic Resonance)



Ayşenur and Arek are presenting docking results



Ayşenur and Fatma are conducting an ITC experiment



Prof. Engin Serpersu
(UTK / ORNL)



Ast. Prof. Salih Özçubukçu
(ODTU Chem. Dep.)

Active Projects



Peptidomics / Transcriptomics

- De-novo sequencing with mass spectroscopy
- cDNA Library based discovery

Activity-Guided Discovery

- Antimicrobial Peptides
- Potassium Ion Channel Blockers
- Anticancer Peptides

Structural Biology / Protein Engineering

- Chlorotoxin (CLTX)

Bioconjugation / Targeting

- CLTX-Quantum Dot

Therapy

- Chronic Lymphocytic Leukemia (CLL)

Collaboration

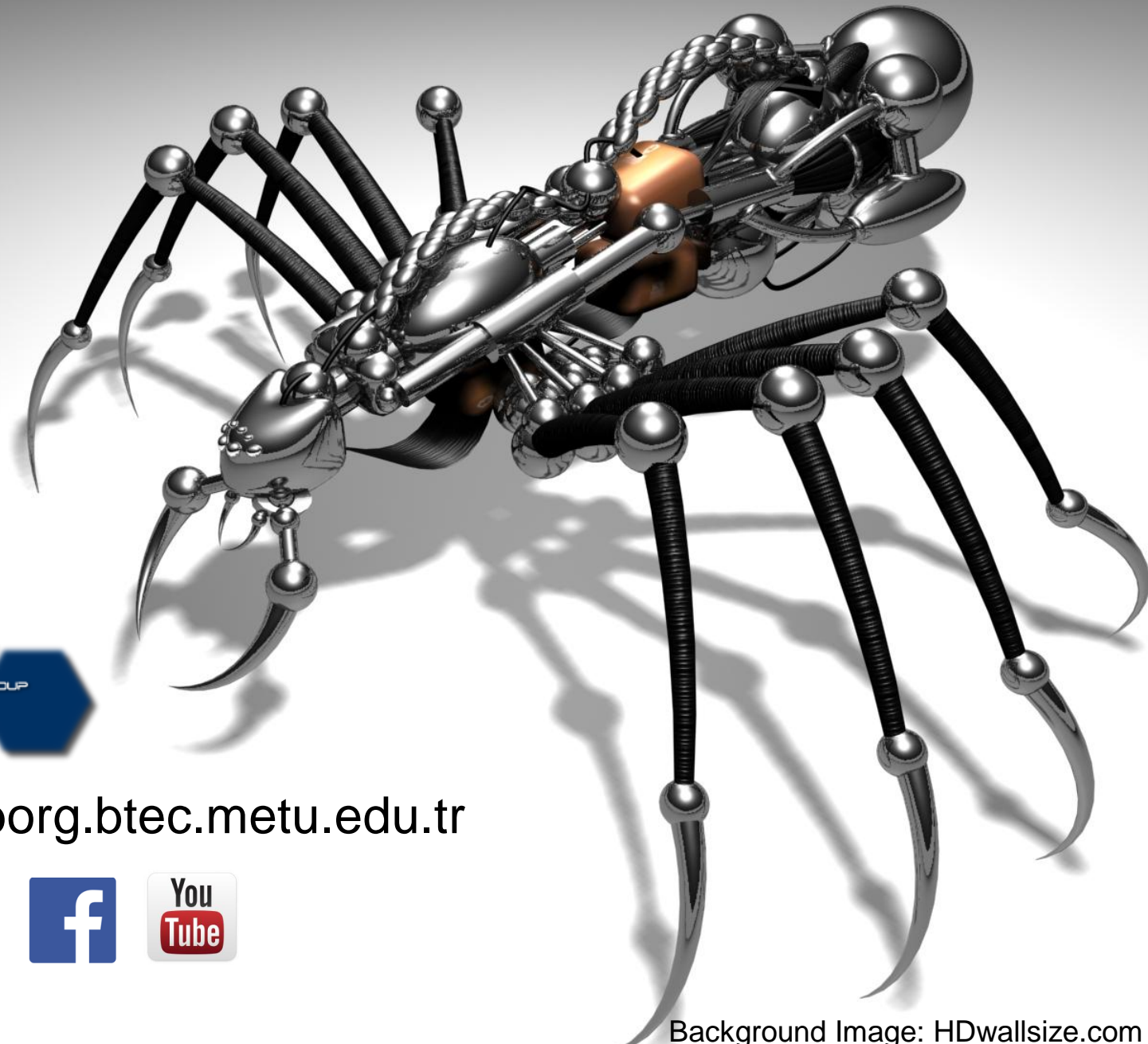


What We Offer

- Rich natural resources > potential lead discovery from endemic species
- Human resources
- Protein biochemistry and bioanalytical method expertise

Seeking Groups with expertise in

- Venom research
- Ion Channels
- Antibiotic discovery



www.syborg.btec.metu.edu.tr



Background Image: HDwallsize.com