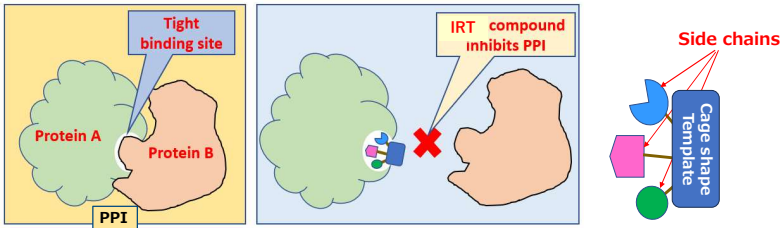


# IRT's Peptide Mimetic Technology

Irimajiri Therapeutics, Inc. (IRT)

## Alkaloid Compound Library System (ACLS)

1. **IRT Technology to inhibit PPI by using peptide mimicking compound which has cage-shape template and rigid side chain direction.**

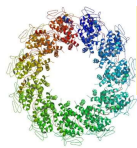


IRT compound inhibits PPI efficiently by covering the key interaction site, which is usually small interface.

2. **Establishment of IRT peptide-mimetic technology -Research into rabies virus inhibitors-**

Oita University's microbiology department has extensively studied the rabies virus.

Inclusion body: This structure is essential for rabies virus growth



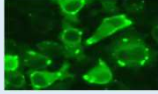
Deletion of 19 amino acids from the N-protein C-terminal domain prevents inclusion body formation

Oita University result

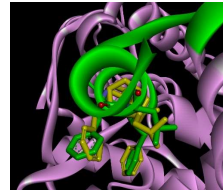
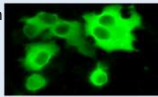
from alanine scan result

**Inclusion body (bright spots)**

Control: Intact rabies virus growth in Neuro-2a cells

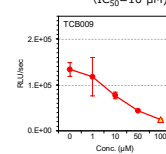


Alanine mutant in 438 (F → A). The formation of inclusion bodies were inhibited.



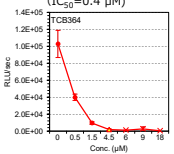
The C-terminal IDP domain (19 amino acids) formed a helical structure in the inclusion body (green), of which three amino acids were shown to be essential by alanine scan

The above compound (yellow) (IC<sub>50</sub>=10 μM)

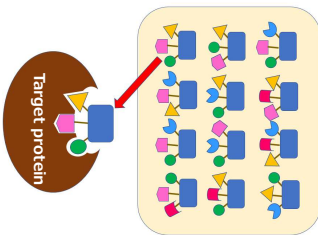


Derivative synthesis

TCB-364 (IC<sub>50</sub>=0.4 μM)



3. **ACLS** consists of compound that are build on 6 different cage shape templates with 3 side chain arms which mimic a part of protein(s).

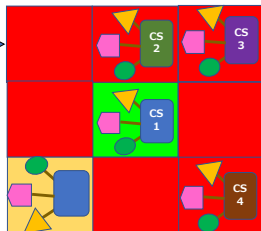
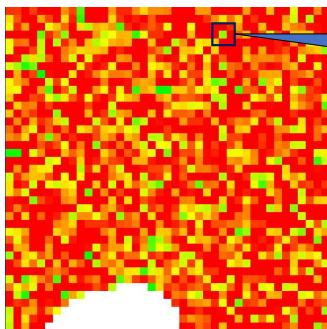


Highly likely one of the compound will interact with target protein

- 10 amino acids which are frequently seen in PPI have been selected.
- Combination of 3 amino acids and 6 different core scaffold - total 6000 compounds



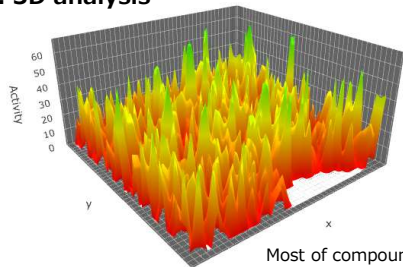
4. **Activity data analysis in ALS targets (SOD1 – Derlin-1)**



- 2000 compounds evaluated includes 4 different cage scaffold (CS-1~4)
- Compound with different scaffold and same side chain showed opposite results (CS-1:positive, CS-2, 3, 4: negative)
- Difference in the angle of the side chains between 4 core scaffold is only 5-10 degrees

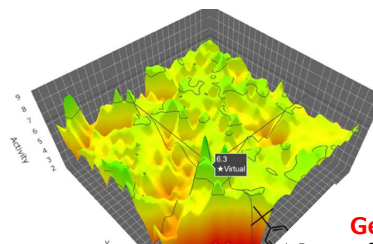
Compounds aligned based on structure similarity. Green as high efficacy, red as no efficacy

5. **3D analysis**



**ACLS**

Most of compounds holding similar structure with hit compound showed low efficacy.



**General Compound Library**

Image of the data based on compounds that are generally used as compound libraries. Compounds with similar structure usually show similar efficacy.

6. **IRT propose:**
- ACLS can be supplied without structure information.
  - When any active compounds are found, IRT can supplied the derivatives of the active compounds.
  - Partner and IRT can jointly file several selective patents.
  - Partner can solely hold the right of their clinical compound(s).