# Your Preferred Knowledgeable CADD Partner

# INDRAS®

*In Silico Discovery Research Academic Research Services Pvt. Ltd.*

44-347/6, Tirumalanagar, Moula Ali, Hyderabad-500040, TS, INDIA


## SREEDHARA RAO, VOLETI, Ph.D

Managing Director

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# Philosophy of INDRAS

***INDRAS*** (R)- A Company Caters

***Rational In Silico Solutions*** To

Organizations Conduct ***Drug Design***

***& Discovery Research***

# Vision and Mission Statement

**VISION : To Promote CADD Utility in Research & Teaching Oriented Organizations, and Generate Clinical Candidates**

**Mission : To Generate Jobs in CADD for At least 10-Scientists by 2020**

# Working Relationship

## INDRAS

- Consult : Expert CADD Consultancy
- Contract : In-source CADD Solutions
- Collaborate: Knowledgeable CADD Research

**With Academia, Institutes, and Industry in Research in Drug Design and Discovery**

# INDRAS Consulting Arrangements

## Consulting Modes:

1. Individual KOL to Clients in Business Meetings
2. Project-based Expert Research Advise
3. Install and Manage CADD Center at Client-Site

# INDRAS Contracting Arrangements

## Contracting Modes:

1. Install and Manage on-site Contract Work

   - Enhanced CADD-Scientist Interactions

2. In-source Client's CADD Project Work

   - Accomplish and Share Timely Research Outcomes

# INDRAS Collaborating Arrangements

## Collaborating Modes:

1. Work in Tandem with Organizations

   - To Facilitate CADD Component in Research Projects of Drug Discovery.

2. Work with Organizations

   - Analyze, Write, and Manage Research Grants Collaborating with Organizations.

# Company Information - INDARAS

- Incorporated - October, 2013
- Location - Hyderabad, TS, India.
- Infrastructure - CADD Computing Hardware
- Expertise – ~20 Years of In Silico Drug Discovery
- Manpower – Turn-key and PhD qualified.

# Founders & Advisor

## Dr. Sreedhara R. VOLETI
Founder – MD/CEO

Dr. Sreedhara Voleti has a PhD in chemistry from Indian Institute of Science (IISc), and postdoctoral research in engineering and biology with and work experience in Pharma R&D of over 20+ years in USA and India. He is a passionate entrepreneur and founded INDRAS & Theraxel Discoveries.

## Mr. Ravikanth S. Bh.
Co-Founder – CFO

Mr. Ravi Kanth has served various business sectors like HR consulting, IT & ITES Outsourcing Services, Oil & Gas Industry products Trading, Agricultural Commodities Trading. At present Mr. Ravi Kanth stays in Malawi working as GM Operations with a reputed Agricultural chemical, Pesticides, Farm Implements.

## Dr. Uday Saxena
Advisor

Dr. Uday Saxena is the Co-Founder of Reagene Innovations. He has held several executive and leadership positions in pharmaceutical industry across the globe. He was associated with the Team at Parke-Davis/Pfizer that discovered Lipitor/atorvastatin, a block buster drug for cardiovascular complications.

# Founder & Promoter

## Dr. Sreedhara R. Voleti, PhD

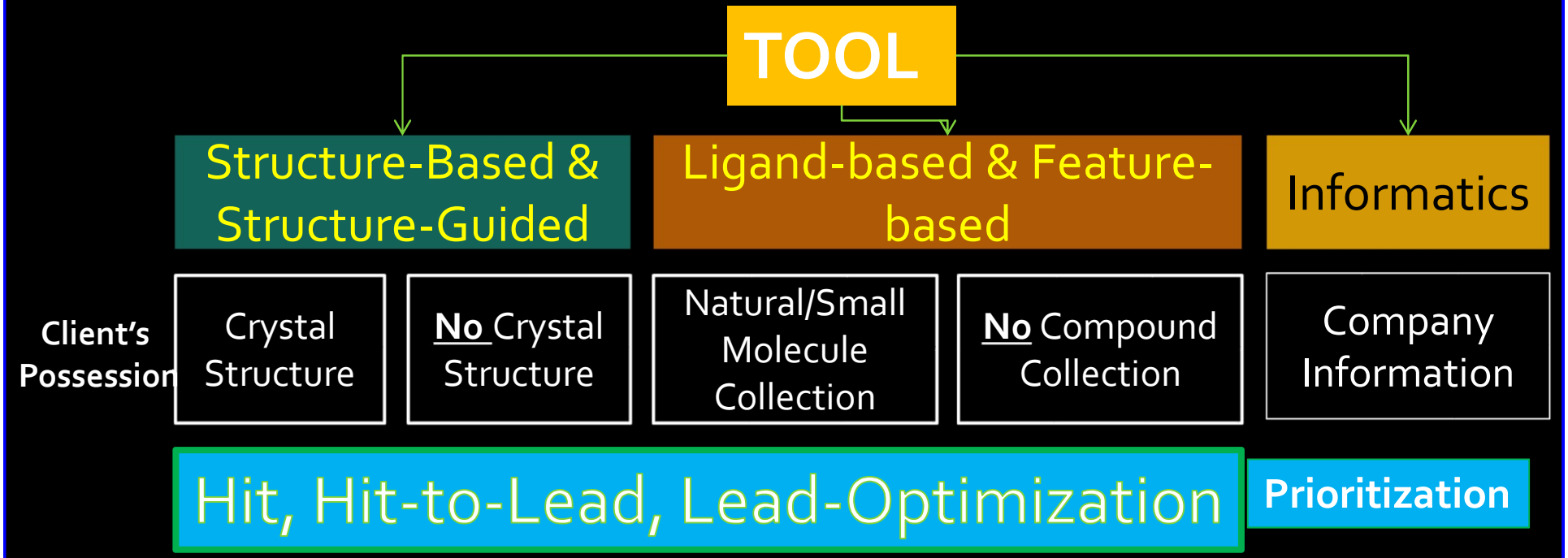
**Founder & Managing Director**

Sree is a specialist researcher in the fields of Molecular Modeling and computer aided drug design/discovery for ~20 years with academic, Pharmaceutical industry, and non-profit organizational settings both in USA and India. He brings valuable research and managerial expertise in this arena. Sree, published, managed, supervised CADD teams, conducted in silico rational drug discovery of various therapeutic areas. He promotes CADD in academic and industry scenario – and he is passionate about teaching, training, and parting research knowledge of CADD.

# Key Career Achievements

- Played Key Role With Med. Chem. Teams in Discovery of MMP9-12, 5LO-H1 dual-inhibitor Clinical Candidates
- Successfully Optimized and Prioritized dual DPP4-ACE Inhibitor That Saved Time/Money/Resources for Research Organization
- Attracted Funding in Designing Selective Subtype PI3K/Mtor Inhibitors For Treatment Of Cancers
- Identified Potential TAK1 Receptor Antagonists as ALTERNATE THERAPY in T2DM
- Successfully Supported Over 30 Research Projects Across Diverse Therapeutic Areas
- Consulted with Camitro Corporation, Inc., now Transformed as OPTIBRIUM, UK.
- Recognized with APPRECIATE Award (Runner Up) by Global Ranbaxy R&D for Successful Data Management to Desktop, Corporate Data Access-to-Desktop Facilitating Over 500 Scientists of R&D

# Key CADD Tools



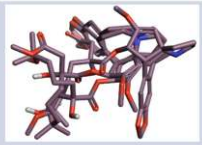
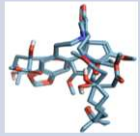
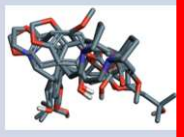
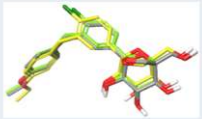
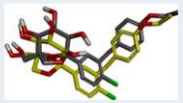
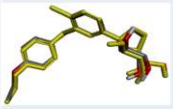
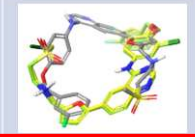
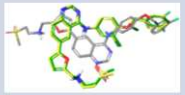
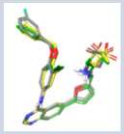
# Case Studies

1. CHEMVEDA Life Sciences & NIPER, Hyd.
2. Connexios Life Sciecnes
3. Glenmark Pvt. Ltd.
4. Incozen Therapeutics Pvt. Ltd.
5. Laxai Avanti Life Sciences Pvt. Ltd.
6. ReaGene Innovations Pvt. Ltd. & Tech Mahindra

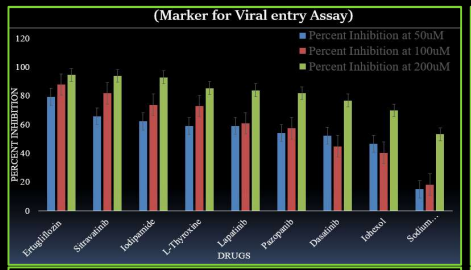
# Drug Repurposing as Therapeutics for COVID-19

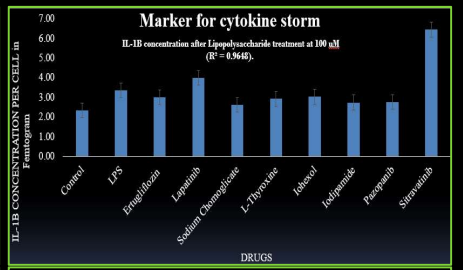
## With ReaGene Innovations Pvt. Ltd. & Tech Mahindra Pvt. Ltd. (2020-2021)

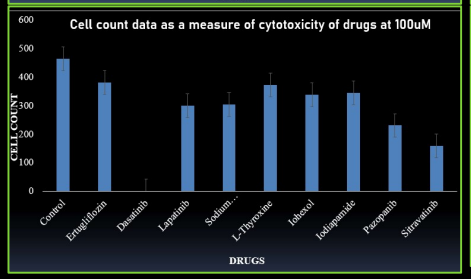
### Conformational Consistency of Top Repurposed Drugs

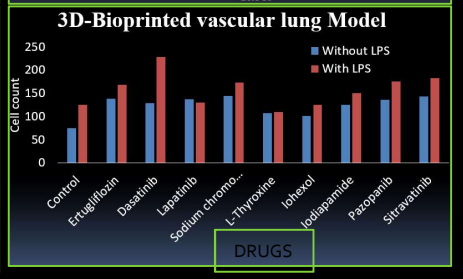
| # | | Mpro Site | S1-1 Site | S1-2 Site |
|---|---|---|---|---|
| 1 | Homo-harringtonine |  |  |  |
| 2 | Ertugliflozin |  |  |  |
| 3 | Lapatinib |  |  |  |

### In Vitro Results of the Prioritized Repurposed Drugs




1. Identification of SGLT2 inhibitor Ertugliflozin as a treatment for COVID-19 using computational and experimental paradigm. BioRxiv **2021.06.18.448921;**

2. Tyrosine Kinase Inhibitor Family of Drugs as Prospective Targeted Therapy for COVID-19 Based on In Silico And 3D-Human Vascular Lung Model Studies, BioRxiv **2021.05.13.**443955

3. In silico and in vitro Demonstration of Homoharrintonine's Antagonism of RBD-ACE2 Binding and itsAnti-inflammatory and anti-thrombogenic Properties in a 3D human vascular lung model, BioRxiv **2021.05.02.442384;**

4. **Mini Review:** Emergence of New Drug Discovery Paradigm using Computational and Experimental Biology, Journal of Infectious Diseases and Diagnosis, Vol.6. iss.2, #152. **(2022)**

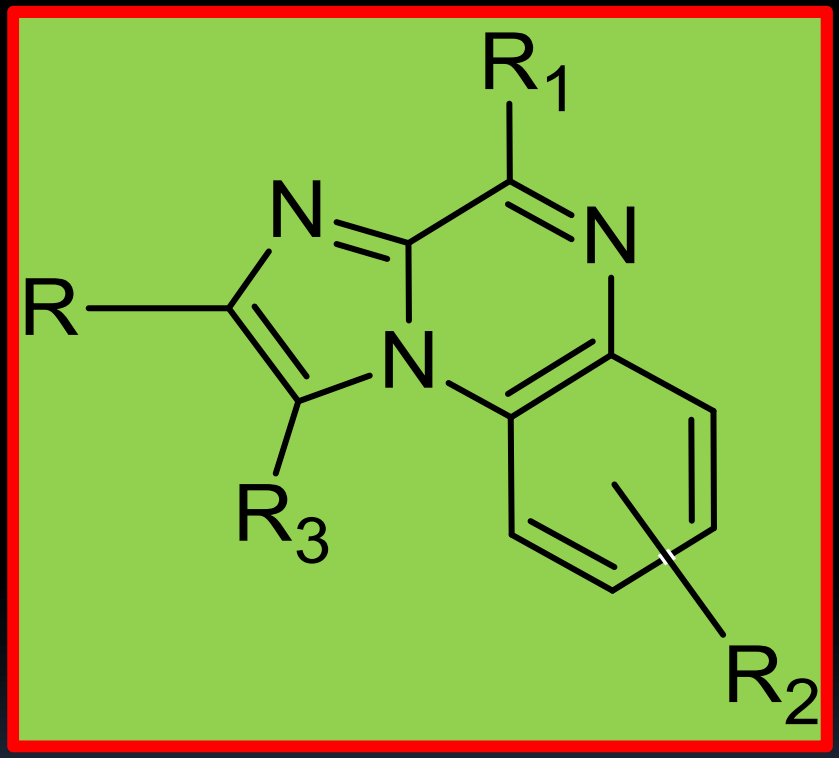
**Patent filed:**

**Rational Identification of FDA Approved Drugs by Computational Modelling and Inhibition of RBD/ACE2 Binding for Treatment of COVID-19**., PCT/IB2021/057470, 13 August 2021

# Designed Selective Inhibitors

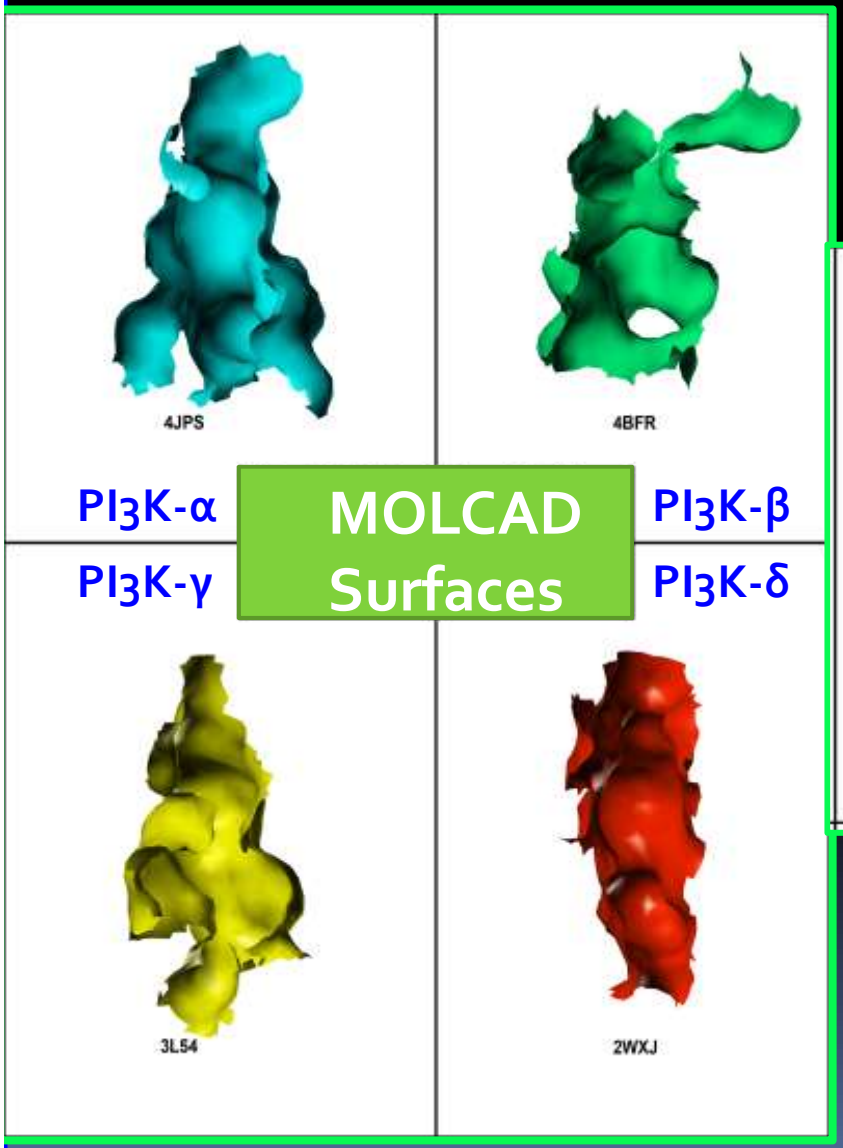
## With CHEMVEDA Life Sciences & NIPER, Hyderabad

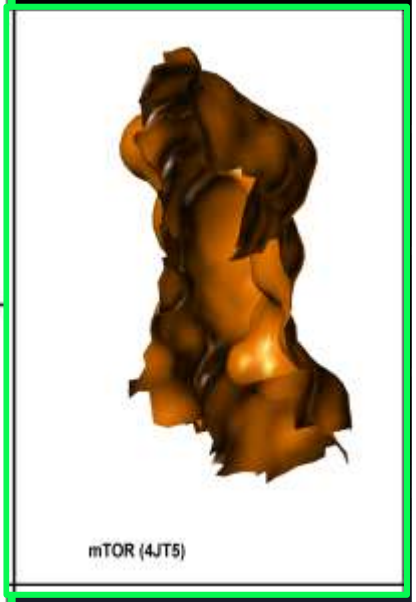
### BIRAC – SBIRI Project (2016-18)




## Designed Selective PI3Kα-, PI3K-β, and dual mTOR-PI3Kα, mTOR-PI3Kβ Inhibitors in Oncology

# Active Sites of PI3K isoforms & mTOR

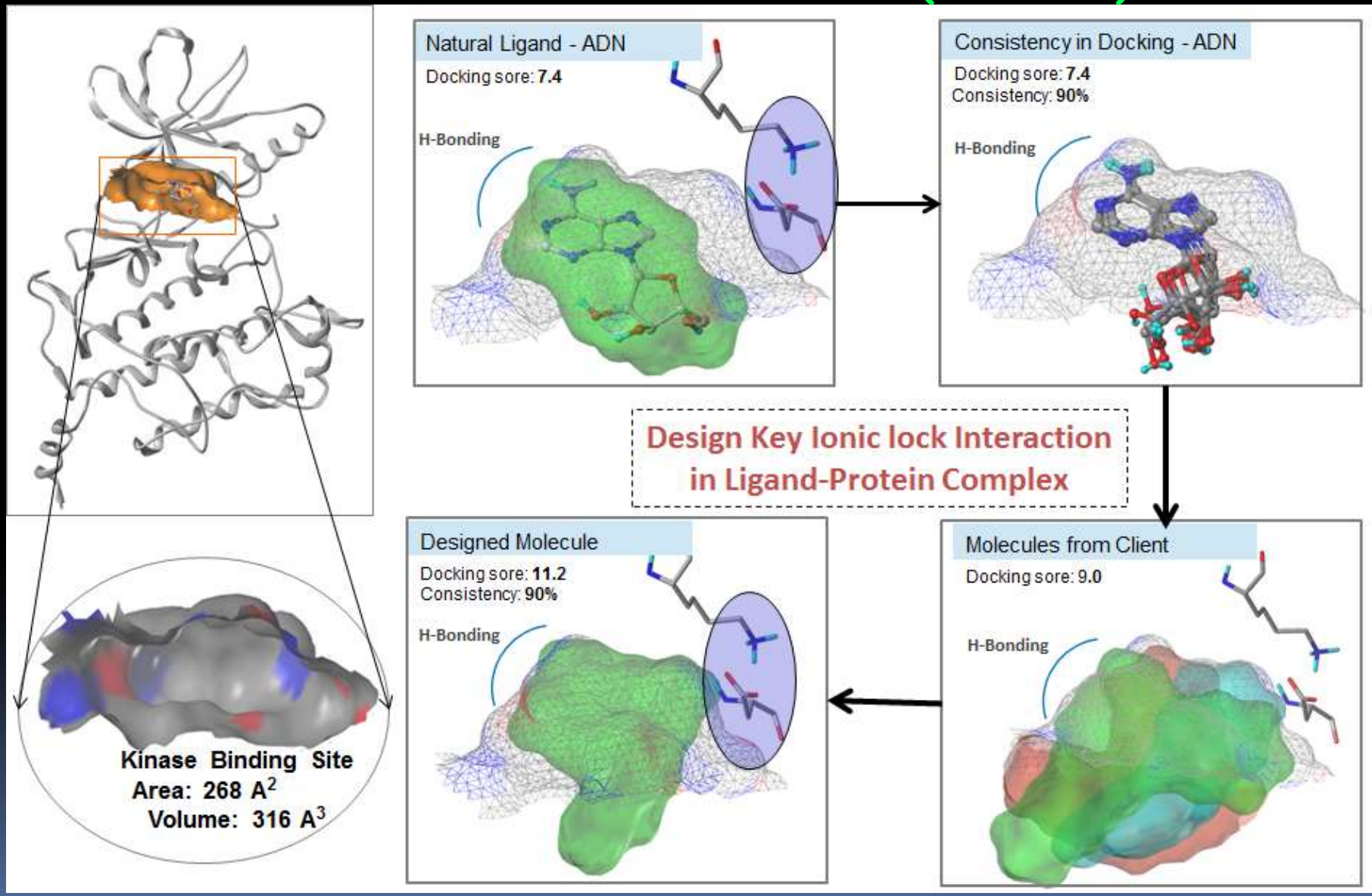



| Kinase (PDB-ID) | Surface Area (Å²) | Cavity Volume (Å³) |
|---|---|---|
| PI3K-α 4JPS | 406 | 445 |
| PI3K-β 4BFR | 475 | 592 |
| PI3K-γ 3L54 | 420 | 531 |
| PI3K-δ 2WXJ | 336 | 430 |
| mTOR 4JT5 | 416 | 521 |

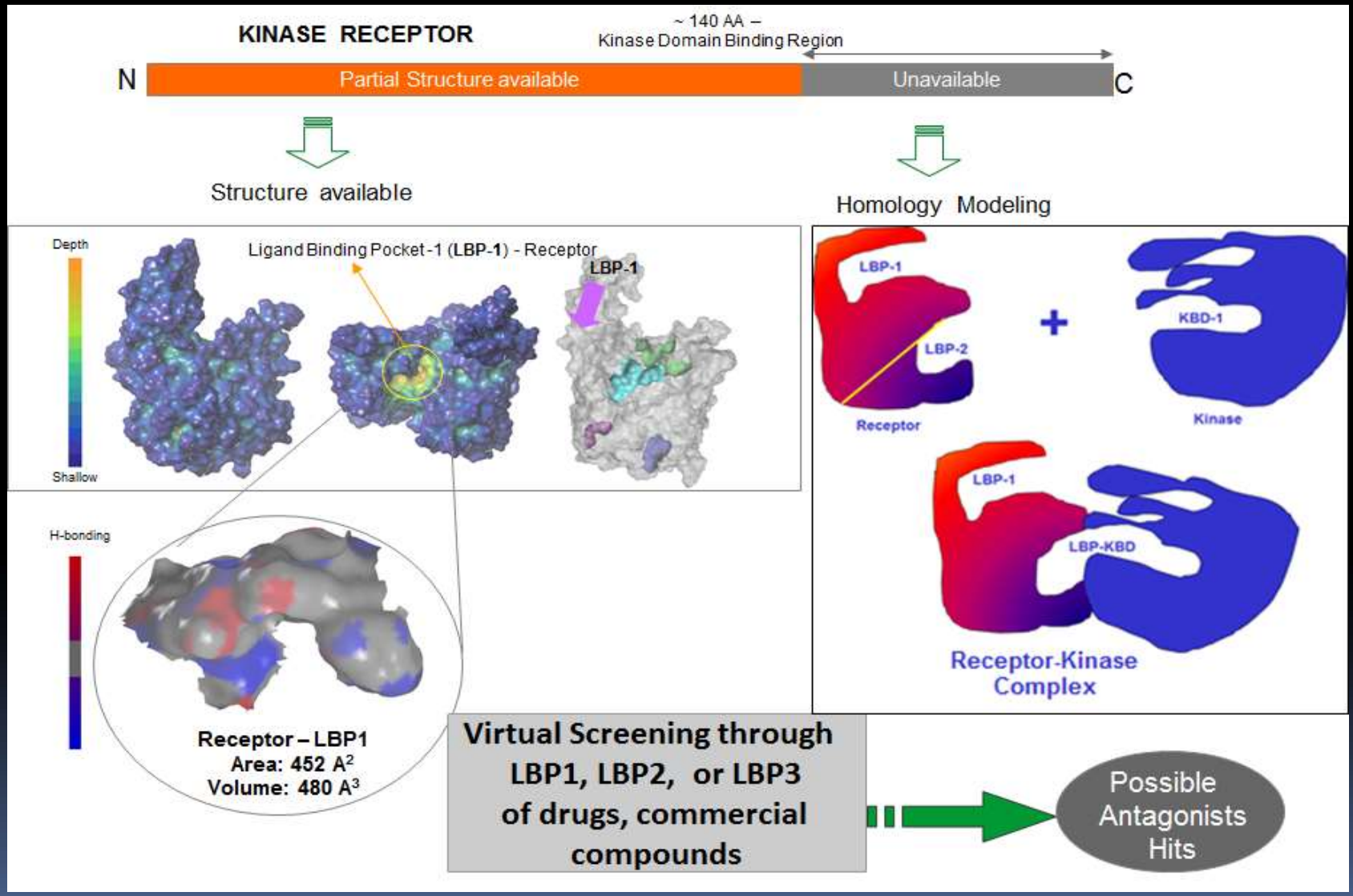
# Design of Inhibitors to TAK1 Kinase Binding site

## With Connexios Life Sciences Pvt. Ltd. (2014-2016)



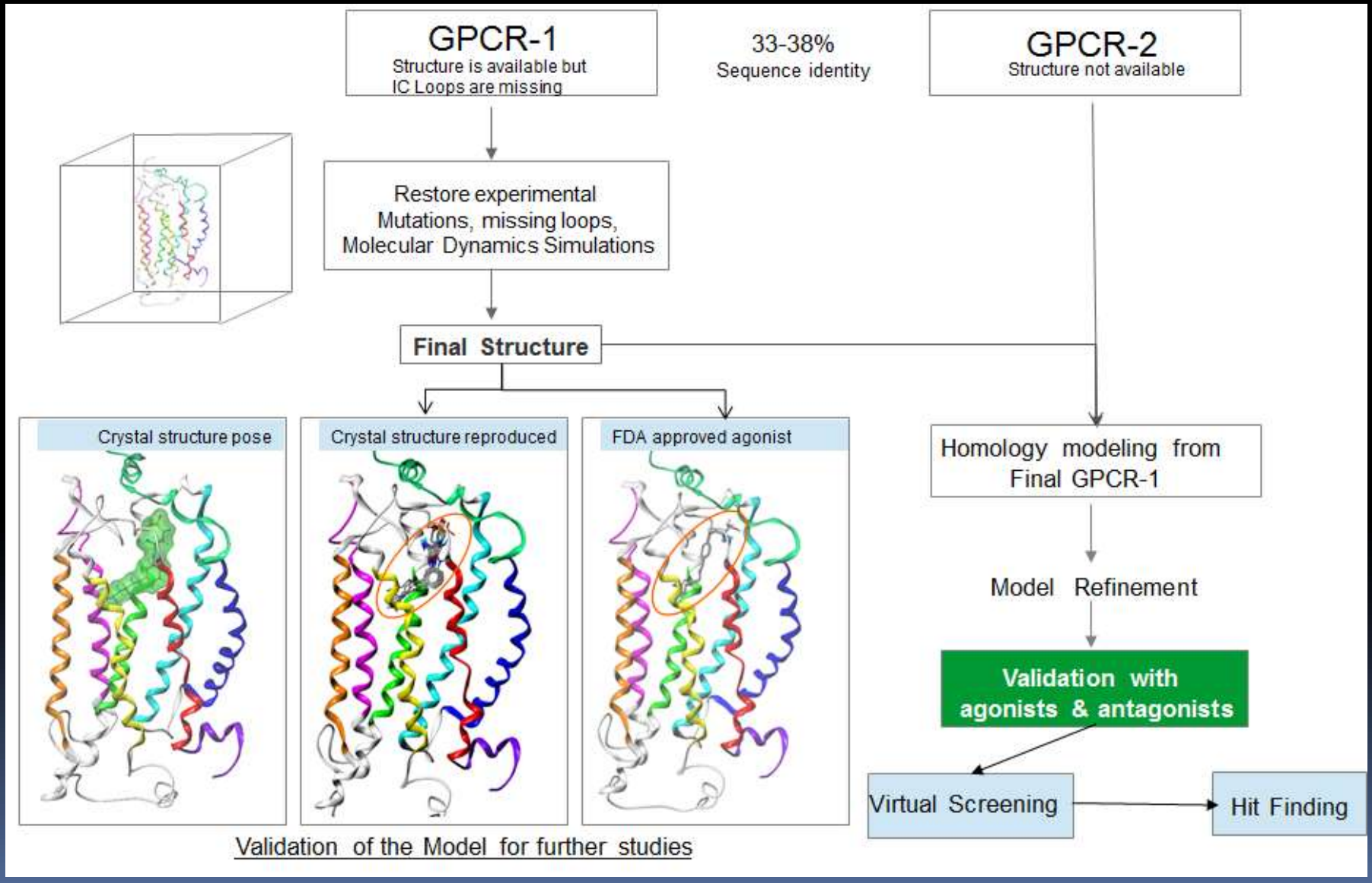
# TAK1 Receptor Complex Antagonists & Virtual HTS

## With Connexios Life Sciences Pvt. Ltd. (2014-2016)



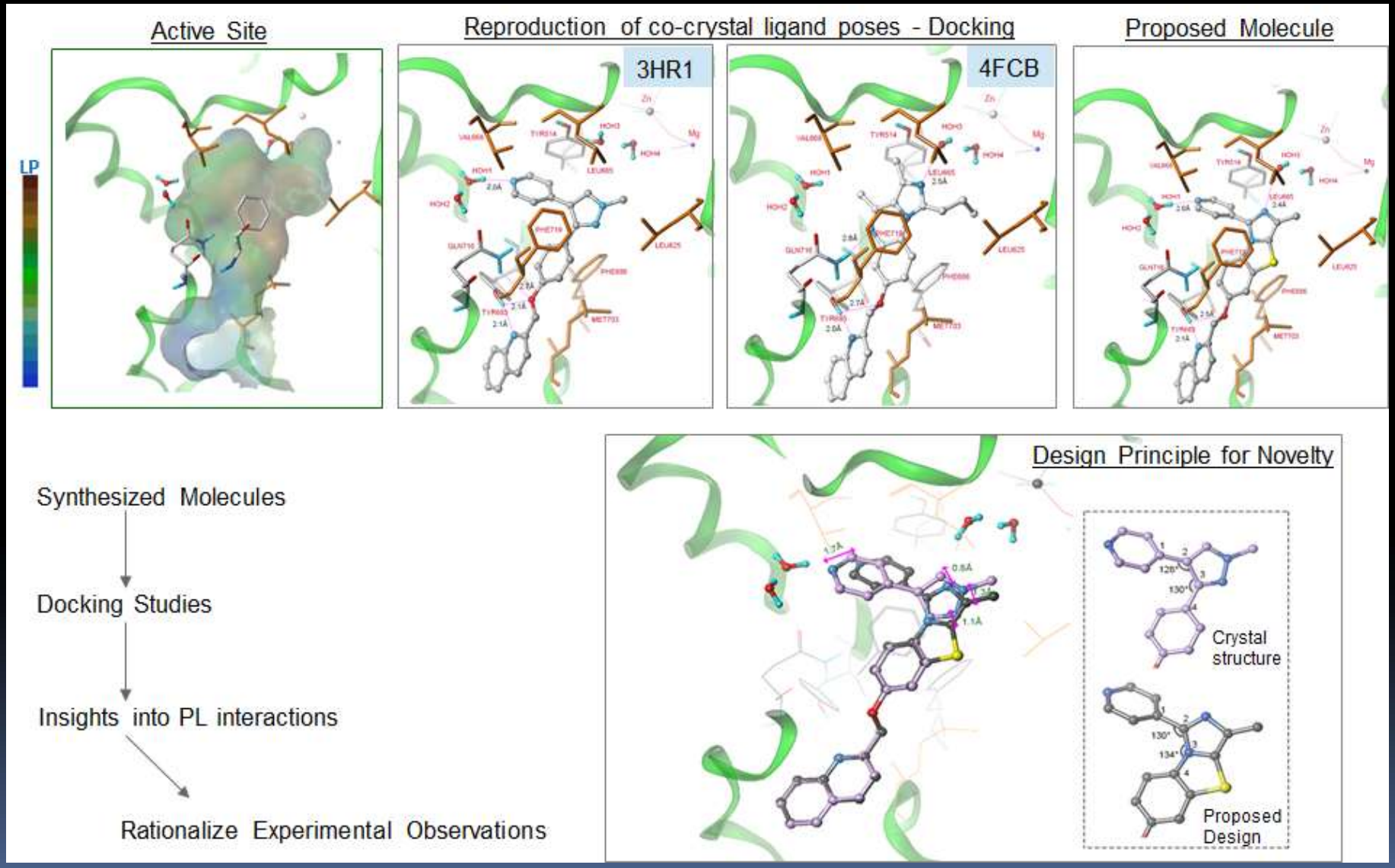
# Modeling GPCRs in Metabolic Disorders

## With Connexios Life Sciences Pvt. Ltd. (2014-2016)



# Rationalize Phosphodiesterase PDE10A Inhibitors

## With GLENMARK Pvt. Ltd. (2014)




Biorg. Med.Chem. Let. 23, (2013) 6747-6754

# Example Slides

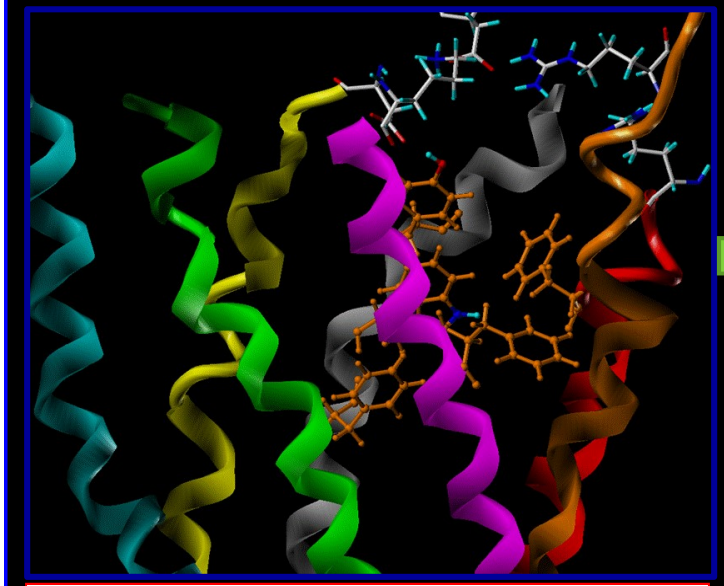
1. Modeling P-L-I in a Single Target (GPCR) - $C_{3a}R$
2. Fragment-based P-L Interactions in an Enzyme - PTP-1B
3. Modeling P-L-I in Dual-action Targets (GPCR-Enzyme) - H1-5LO
4. vHTS in an anti-bacterial Target – Gyr-B
5. Modeling & vHTS for an anti-tuberculosis (*MTb*) Target - CM

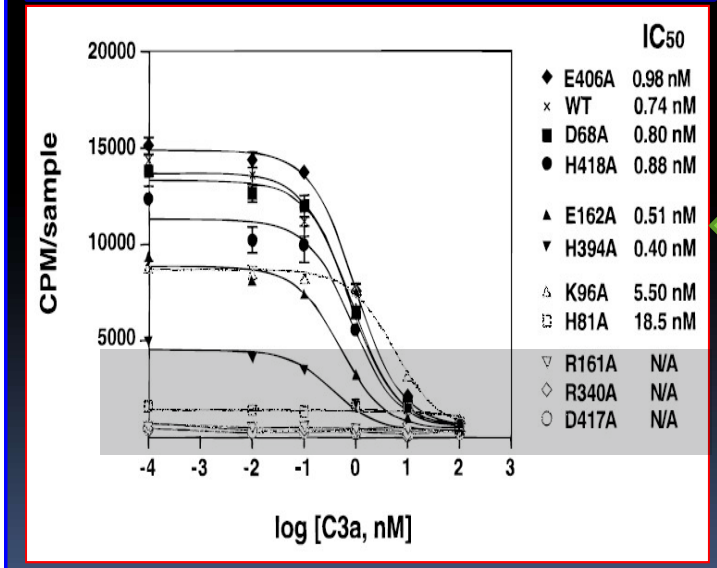
P-L-I : Protein Ligand Interactions
vHTS:- virtual Highthroughput Screening
GPCR: g-Protein Coupled Receptor

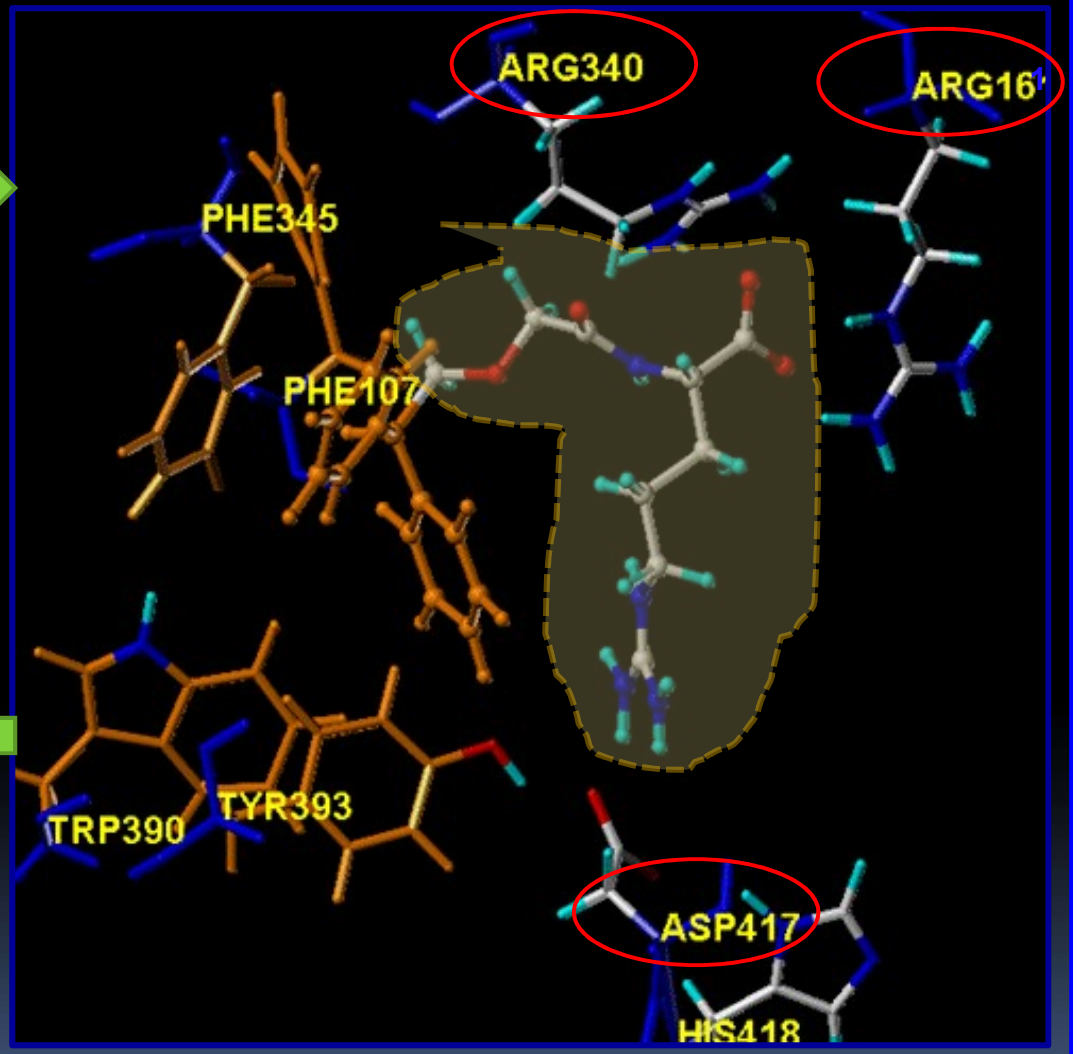
mTb: mycobacterium Tuberculosis
PTP-1B: Protein-tyrosine phosphatase 1B
Gyr-B: Gyrase-B CM :- Chorismate Mutase

5LO : 5-Lipoxygenase
H1 – Histamine-1

# Case Study I – GPCR – C3aR & Rationalized Interactions

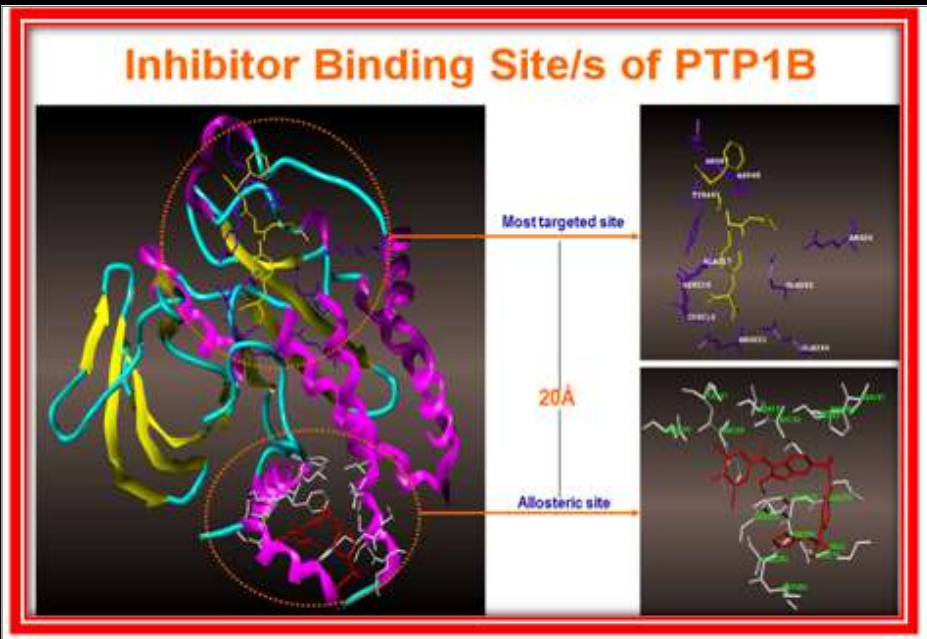


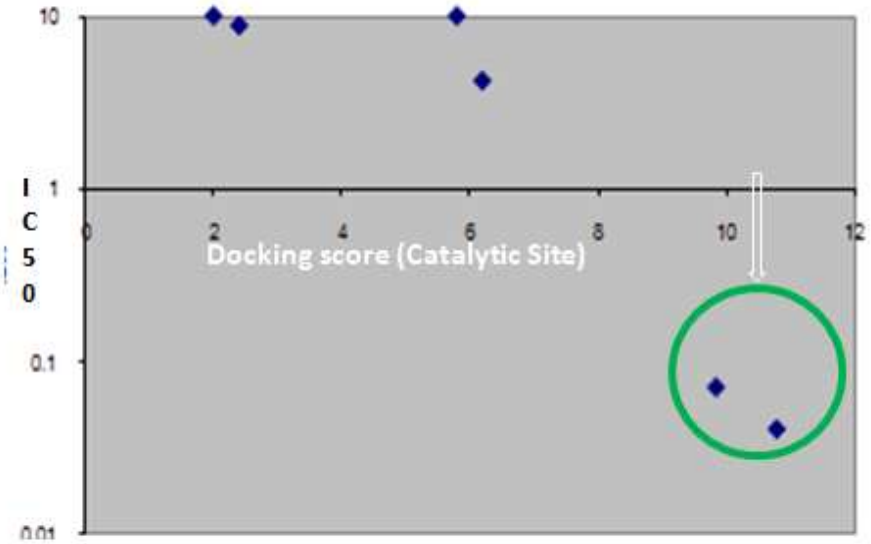


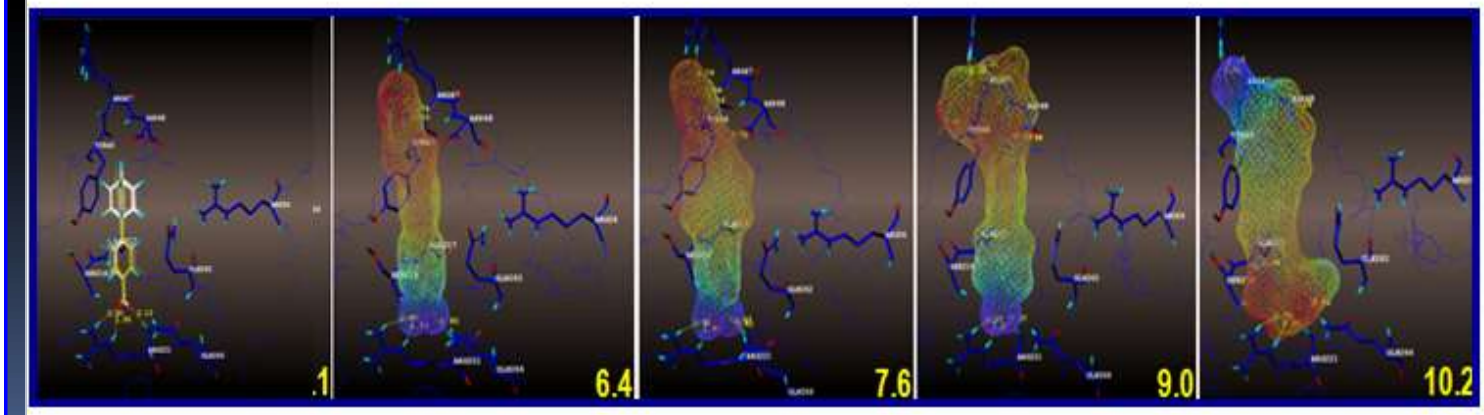



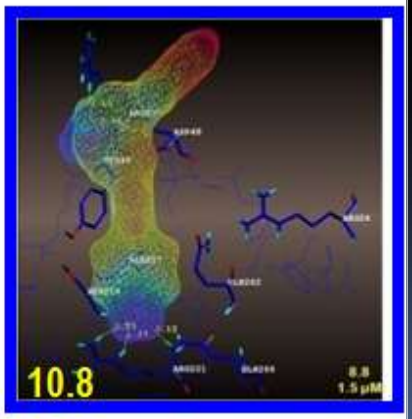

Voleti S.R., *Int. J. Drug Disc.*, 1, 128-136 (2012)

# Case Study II – Enzyme (PTP-1B)



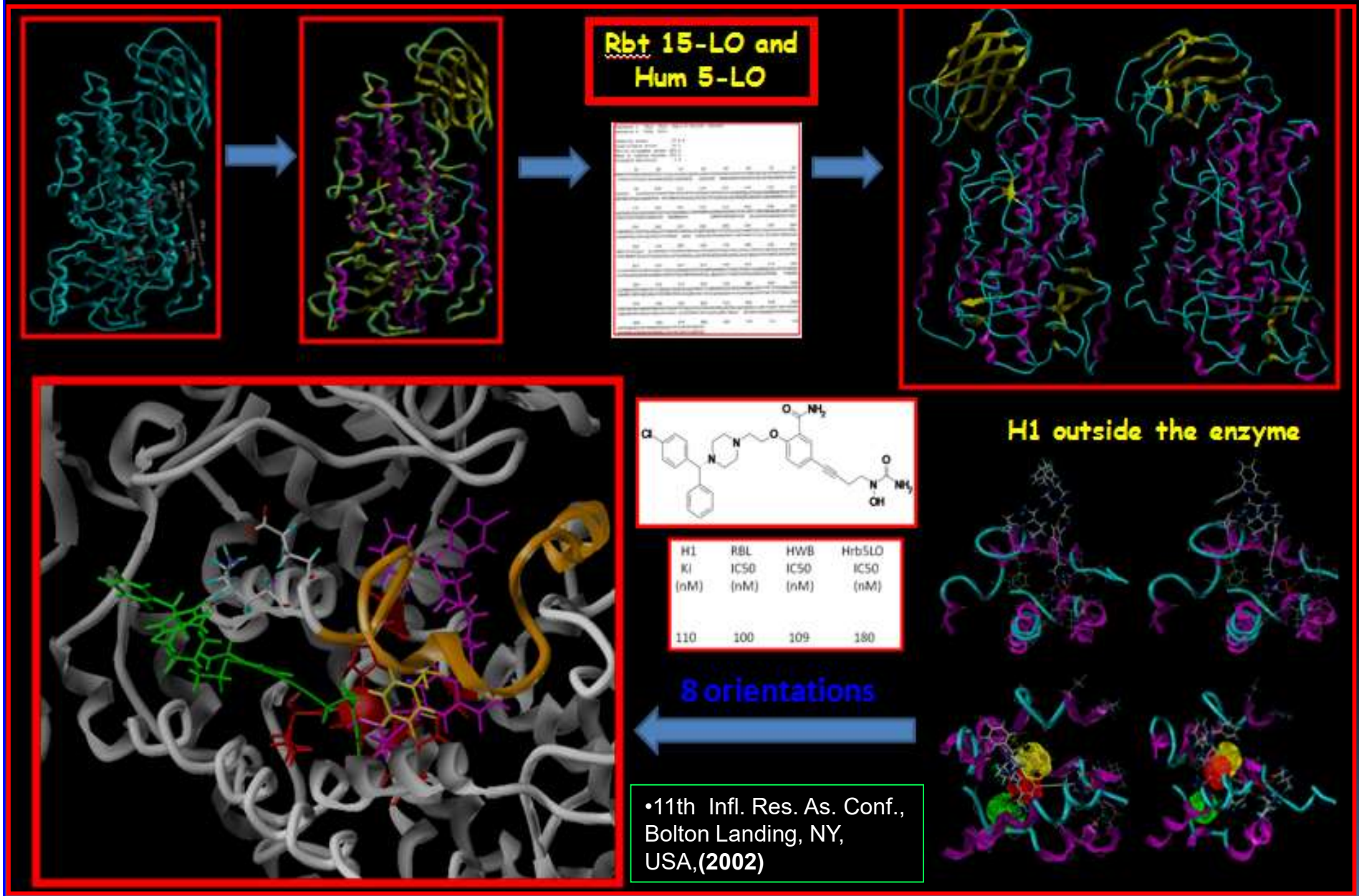




**DST Funded Project: SR-S1-OC-03/2010) – INR 5.4Mn**

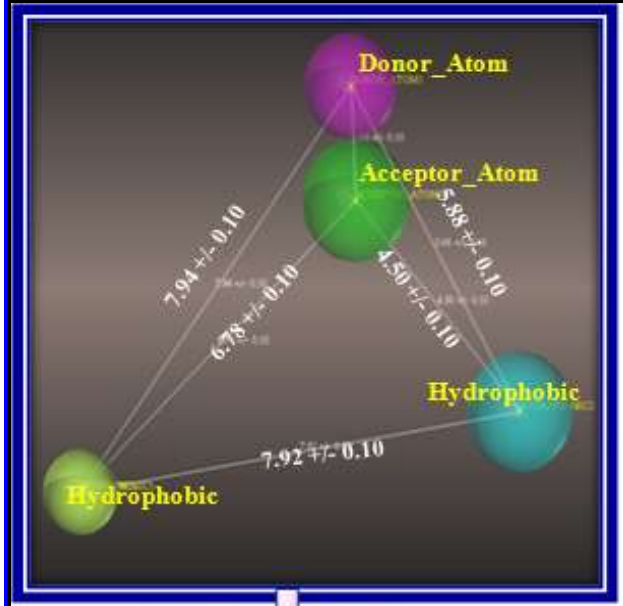
# Case Study III – GPCR and Enzyme (H1-5LO)

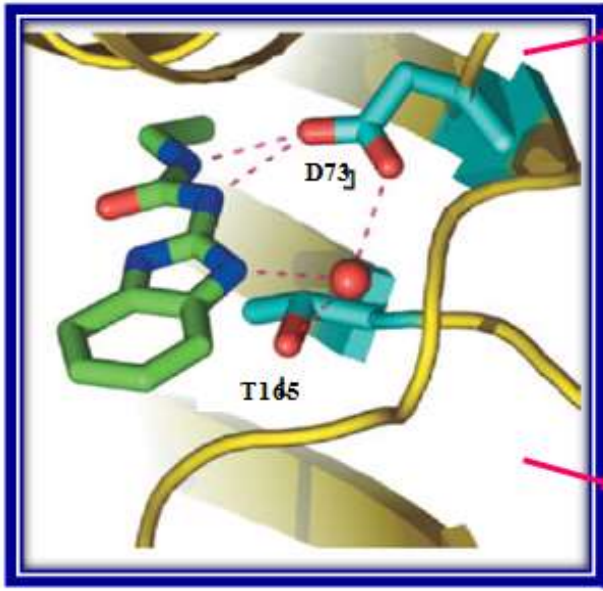


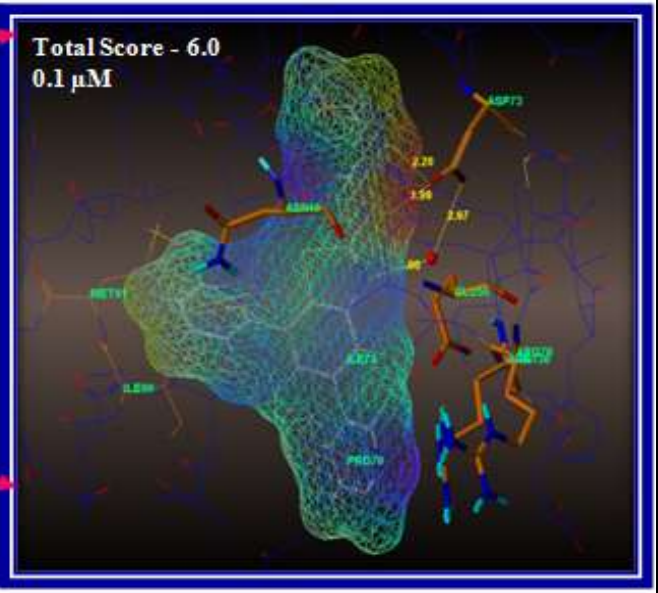

| H1 KI (nM) | RBL IC50 (nM) | HWB IC50 (nM) | Hrb5LO IC50 (nM) |
|---|---|---|---|
| 110 | 100 | 109 | 180 |

•11th Infl. Res. As. Conf., Bolton Landing, NY, USA,**(2002)**

# Case Study IV – Multi-CADD tool Screening (GyrB)



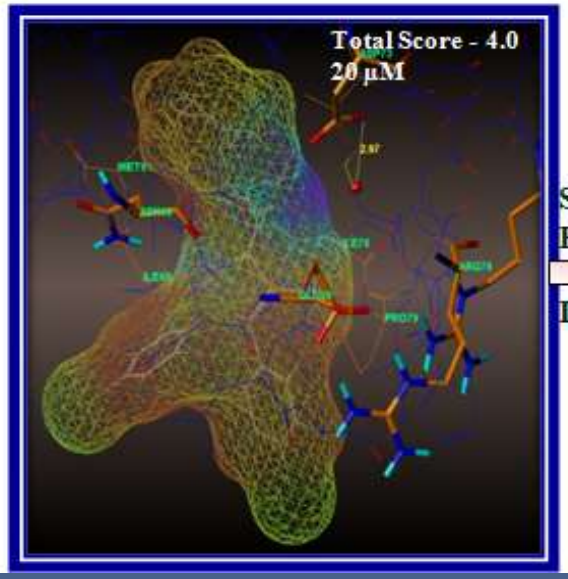




Various filters

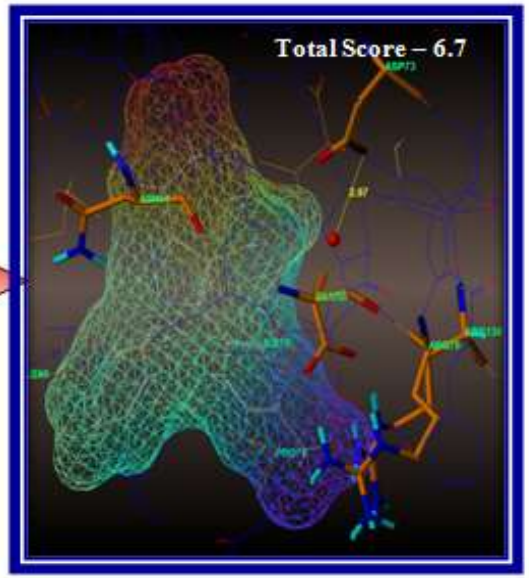
Databases Searching

Molecular Docking / Torsional Minimization / QFIT

Hits




Structure Based Lead Opt.



# Case Study V – Multi-CADD tool Screening (CM in mTb)

Databases → ZINC + COCOCO

~10.3 Mn

Pharmacophores screening

56106

Selection based on fitness value

900 molecules

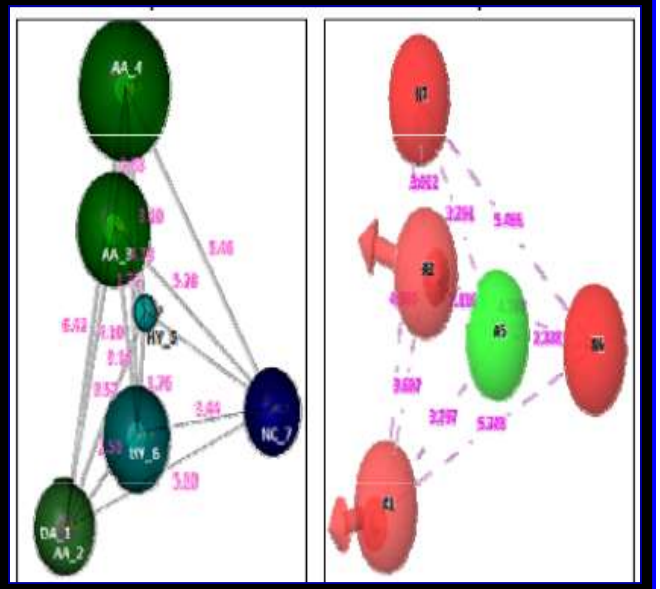
Screening based on docking

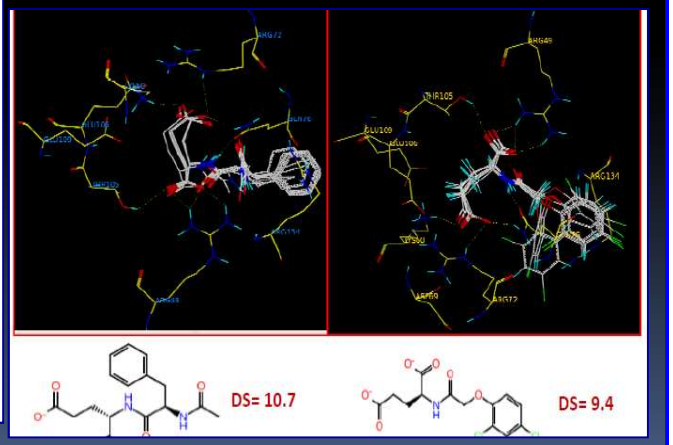
602 molecules

Common high scoring compounds in maestro and sybyl

112 molecules

Select Synthetically feasible molecules and fragments

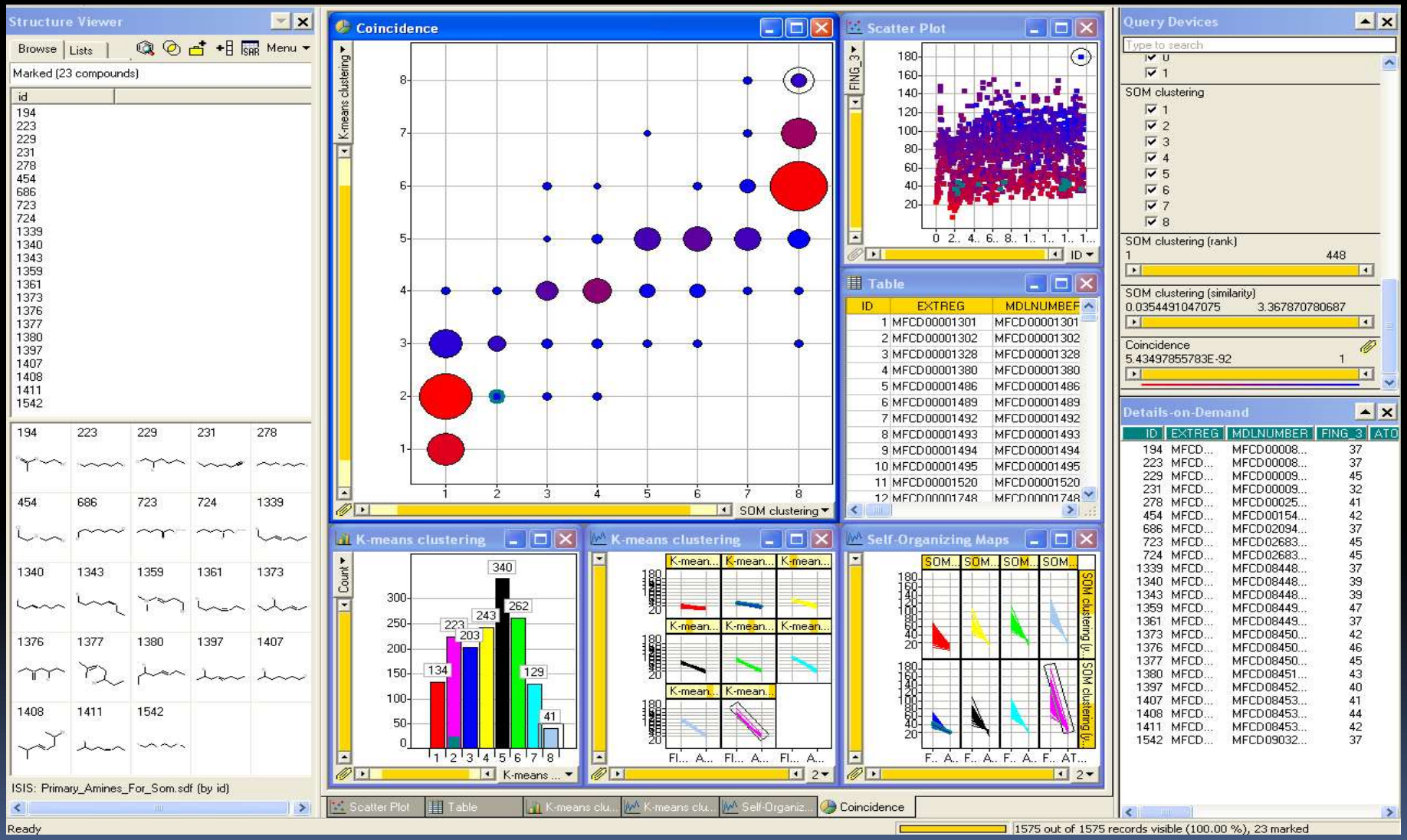





Co-PI: DBT's Centre for Excellence in TB (ILS, Hyderabad)

# Informatics Capabilities

## Cheminformatics - Data Management & Visualization



# Your Partner for Rational Drug Design/Discovery


INDRAS

Insilico Discovery Research Academic Services Pvt. Ltd.

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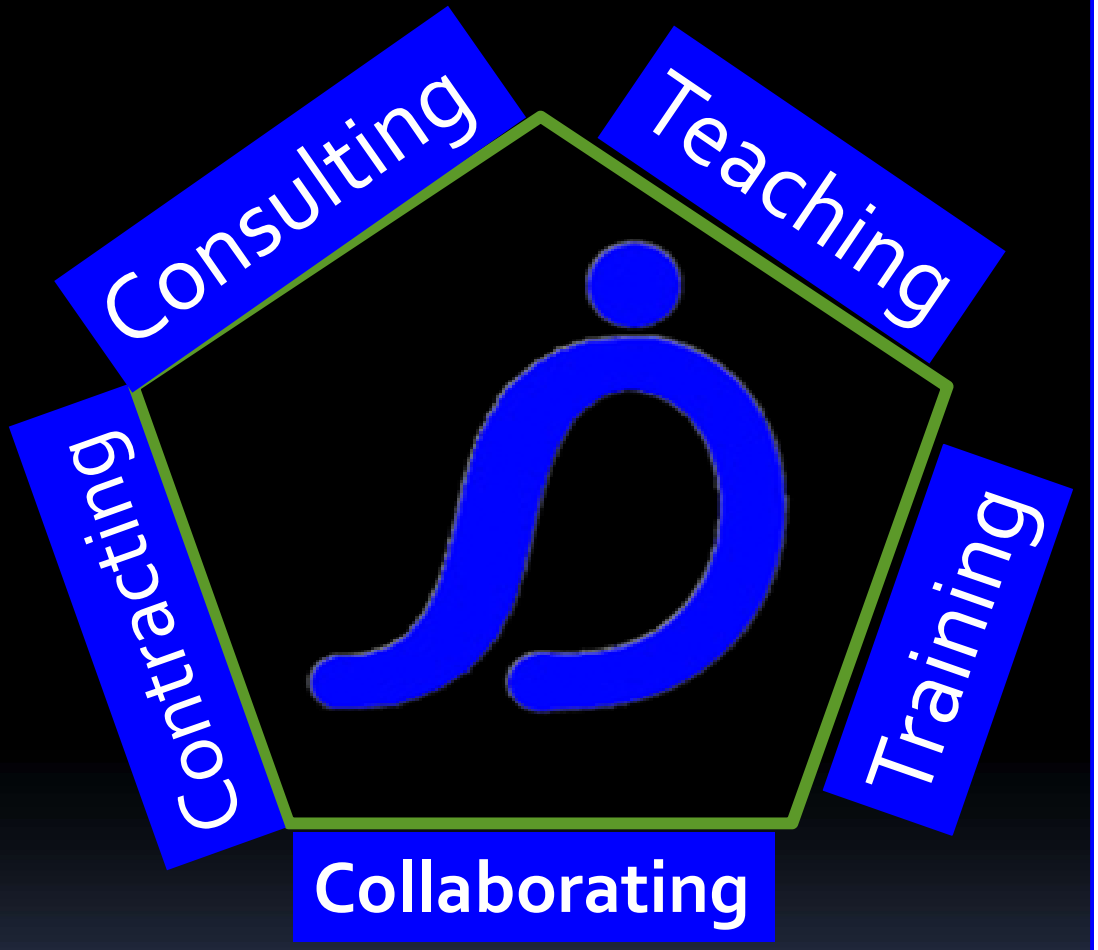


Thank You!