Statement of Research Achievements

Nominee's (Professor Chiranjib Chakraborty) primary research focus is 'Medical Bioinformatics.' Broadly, Nominee attempted to use computational biology to unfold the mechanism of the disease and contribute to therapeutic development. Dr Chakraborty's group has successfully handled more than INR 5000000 funding from all significant funding agencies (private /in-house financing or others).

MAIN RESEARCH AREAS:

His research area is primarily confined to the three directions
(i) Mutation in diseases development, drug resistance, and the creation of virus variants
(ii) The role of ncRNA (noncodingRNA), especially miRNA, in various diseases such as diabetes, cancer, rheumatoid arthritis, etc.
(iii) Immunoinformatics bases vaccine construct development

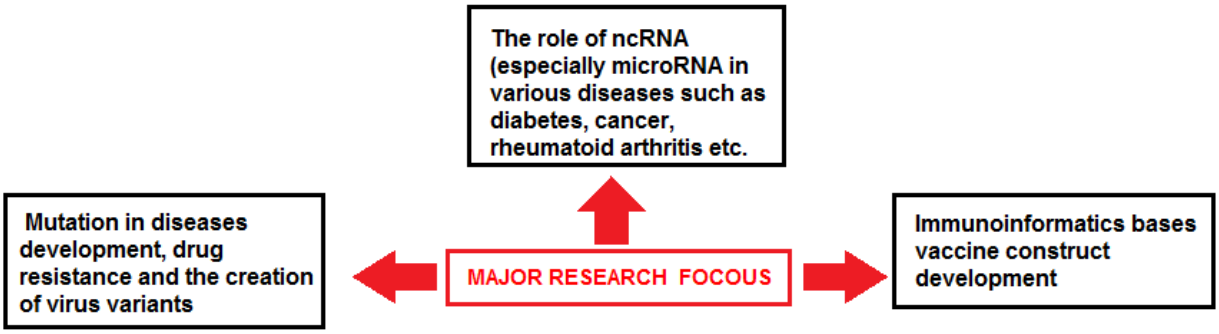

Fig.1. Graphical abstract of my major research focus

OTHER RESEARCH AREAS

His other research areas are following
1. Diabetes, Human CRP (C reactive protein), Cancer, Bone biology,
2. ncRNA/ miRNA analysis
4. Therapeutic discovery
5. COVID-19 and Immunoinformatics
6. Development of in silico based vaccine candidates

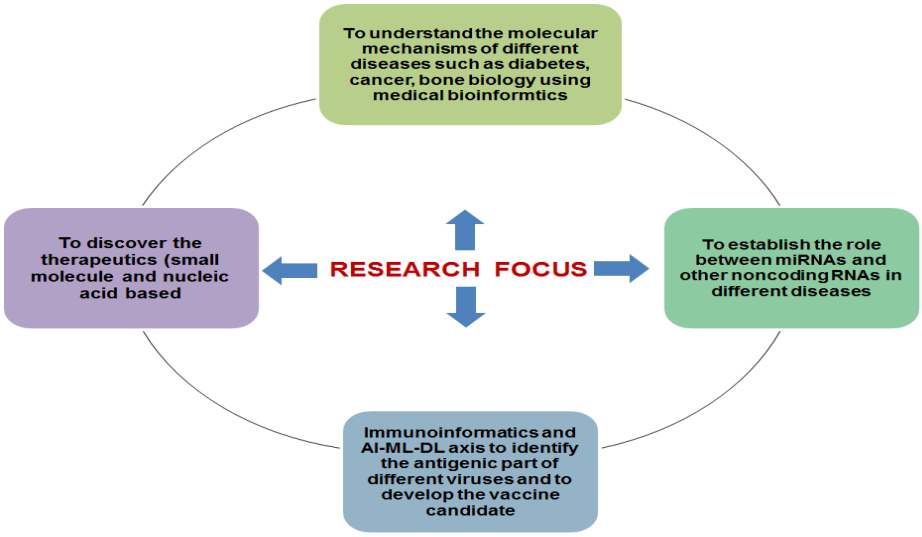

Fig.2. Graphical abstract of Chakraborty's secondary research focus

MAJOR RESEARCH CONTRIBUTIONS

His significant research contributions are as follows:

1. Mutation in diseases development, drug resistance, and the creation of virus variants

1.1 . Mutation in Diseases: Structural Glucokinase (GCK)Mutation Causes MODY 2

GCK (glycolytic enzyme glucokinase) mutations can consequence in an autosomal dominant hereditary illness. It causes MODY 2 (maturity-onset diabetes of the young, type 2). The study investigated missense mutations in the GCK. The study identified three significant mutations(E70K, A188T, and W257R). These mutations were noted as highly deleterious using high computational prediction scores. The models were developed for the proteins with mutations which were designed derived from the crystal GCK protein structure. MD simulation was performed to demonstrate the surface properties change of native and mutant proteins. The study correlated MD simulation and structural changes.

Publication: Theranostics 4(4):366-385. **IF: 12.4** [https://pubmed.ncbi.nlm.nih.gov/24578721/] (**More than 56 citations)**

1.2. Mutation in Drug Resistance: G719S-T790M Double Mutation in the EGFR Kinase Domain Causes Therapeutics Resistance

EGFR is one of the therapeutic targets for NSCLC (non-small-cell lung cancer). The study tried to understand the resistance to the EGFR-specific antibody gefitinib. The double mutation (DM) G719S and T790M were causing the conformational change of EGFR. It might occur due to the combination of mutations (G719S and T790M). The study has shown DM's structural influence and impact of G719S/T790M in EGFR with ligand (gefitinib) through docking and MD simulation

analysis. The study found an increase in distance between the activation and functional loops due to the mutation T790M compared to the mutation G719S. At the same time, it was noted that T790M might cause the ligand to escape from the pocket (binding pocket), whereas G719S assists the ligand in shifting closer in the hinge region.

Publication: Doss CGP, Rajith B, **Chakraboty C**, Naga Sundaram N, Shabana Kouser Ali, Zhu H (2014) Structural signature of the G719S-T790M double mutation in the EGFR kinase domain and its response to inhibitors. **Scientific Reports** 4: 5868 | DOI: 10.1038/srep05868 **IF: 4.6** [https://pubmed.ncbi.nlm.nih.gov/25091415/] **(More than 46 citations)**

1.3. Mutation in Drug Resistance: Role of Mutations in PfATP6 Artemisinin Resistance for Malaria

PfATP6, a SERCA-type Ca2+-ATPase enzyme, is observed in the malaria parasite. It is a significant protein target for artemisinin. The study analyzed the binding affinity and efficacy between PfATP6 and artemisinin. The study demonstrates the role of mutations in PfATP6 (especially L263K and L263E). It showed that the binding affinity was affected due to the mutation/mutations. The study also found novel compounds that offered a good result for the critical relationship with the mutant protein.

Publication: Nagasundaram N, George Priya Doss C, Chakraborty C, Karthick V, Thirumal Kumar D, Balaji V, Siva R, Lu A, Zhang G, Zhu H. (2016) Mechanism of artemisinin resistance for malaria PfATP6 L263 mutations and discovering potential antimalarials: An integrated computational approach. **Scientific Reports** 6:30106.
IF: 4.6 [https://pubmed.ncbi.nlm.nih.gov/27471101/] **(More than 38 citations)**

1.4. Mutation and Virus Variants: Evolution and Mutational Landscape of Newly Emerging SARS-CoV-2 Variants

The research work describes the evolution of emerging variants of SARS-CoV-2, their mutational landscape, and their transmission approach. The VOCs (B.1.617.2, B.1.1.7, B.1.351, and P.1) and the significant VOIs were illustrated in that direction along with their mutations. The significant mutations were critically evaluated in VOCs and VOIs.The structural landscape of important spike protein mutations (E484K, K417T/N, N501Y, and D614G) has been discussed, impacting public health.

Publication: Chakraborty C*, Sharma AR, Bhattacharya M, Agoramoorthy G and Lee SS* (2021) Newly emerging SARS-CoV-2 variants, evolution, their mode of transmission and mutational landscape. **mBio** 12(4):e0114021. doi: 10.1128/mBio.01140-21 (*Corresponding Author) **IF: 6.4** [https://pubmed.ncbi.nlm.nih.gov/34465019/] **(More than 55 citations)**

1.5. Mutation and Virus Variants: Understanding Mutations in the Genome, S-Glycoprotein, and Antibody Binding Regions of the Omicron Variant

This research describes the significant mutations in the Omicron variant. The analysis illustrated the mutations in S-glycoprotein, other genomic parts, and antibody binding regions. The study identifies the mutations in the antibody-binding region, which includes Y505H, N501Y, Q498R, Q493K, E484A, and K417N. It also detects several mutations near the antibody-binding area N440K, G446S, G496S, T478K, and S477N. The study illustrated the consequence of major

antibody-binding mutations (K417N, T478K, E484A, and N501Y), the effect on antibody affinity, the possibility of amino acid substitution, and the stability of ACE2 interaction.

Publication: Bhattacharya M#, Sharma AR, Dhama K, Agoramoorthy G, **Chakraborty C*#** (2022) Omicron variant (B.1.1.529) of SARS-CoV-2: Understanding mutations in the genome, S-glycoprotein, and antibody binding regions. **GeroScience** doi: 10.1007/s11357-022-00532-4 (*Corresponding Author) **IF: 5.6** (# equally contributed) [https://pubmed.ncbi.nlm.nih.gov/35258772/] **(More than 41 citations)**

1.6. Mutations of o virus: variant Understanding the Mutations of SARS-CoV-2 Omicron

The study illustrated the effect of diverse mutations in antibody-binding regions of the S-protein on the binding affinity of the investigated antibodies. Eight significant mutations in Omicron were chosen, which are D614G, E484A, N501Y, Q493K, K417N, S477N, and Y505H G496S, and seven of them are located in the RBD region. A comparative analysis of the ΔΔG score of these mutations was performed to understand the stabilizing or destabilizing properties of the investigated mutations. It provides information on the SARS-CoV-2 variant, Omicron, on the mutational pattern and exciting properties of these eight significant mutations, such as antibody escape and infectivity.

Publication: Chakraborty C, Bhattacharya M, Sharma AR, Mallik B. (2022) Omicron (B.1.1.529) - A new heavily mutated variant: Mapped location and probable properties of its mutations with an emphasis on S-glycoprotein. **International Journal of Biological Macromolecules** 219:980-997.
[https://pubmed.ncbi.nlm.nih.gov/35952818/]**IF: 8.2 (More than 18 citations)**

1.7. Positive Selection and Mutation: D614G mutation and SARS-CoV-2 Variants

The work concluded from the analyses that the D614G mutation occurs in all the emerging variants (both VOCs and VOIs) of SARS-CoV-2 with high frequency. At the same time, D614G mutation in SARS-CoV-2 variants circulates globally, increasing viral fitness. It was concluded here that the D614G mutation is not a result of genetic drift. It has appeared as a part of the positive selection.

Publication: Chakraborty C*, Saha A, Sharma AR, Bhattacharya M, Lee SS*, Agoramoorthy G* (2021) D614G mutation eventuates in all VOI and VOC in SARS-CoV-2: Is it part of the positive selection pioneered by Darwin? **Molecular Therapy-Nucleic Acids** 26:237-241 10.1016/j.omtn.2021.07.011 (*Corresponding Author) **IF: 8.8 (More than 38 citations)**

1.8. Natural selection of the D614G mutation in SARS-CoV-2 Omicron (B.1.1.529) variant and its subvariants.

The article discusses the high prevalence of the D614G mutation in the SARS-CoV-2 Omicron (B.1.1.529) variant and its subvariants. The D614G might have a selective advantage. At the same time, the mutation might augment the viral fitness.
Publication: Chakraborty C, Saha A, Bhattacharya M, Dhama K, Agoramoorthy G (2023) Natural selection of the D614G mutation in SARS-CoV-2 Omicron (B.1.1.529) variant and its subvariants. Molecular Therapy - Nucleic Acids. 23: 437-439. doi:10.1016/j.omtn.2023.01.013 **IF: 8.8** (*Corresponding Author) **(More than 1 citations)**

1.9. Resistance to nirmatrelvir due to mutations in the Mpro in the subvariants of SARS-CoV-2 Omicron: another concern?

The article discusses the nirmatrelvir due to mutations in the Mpro in the subvariants of SARS-CoV-2 Omicron. The reported significant mutations in Mpro are T21I, L50F, N142L, E166 M/V, Q189E/I, Q192T, P252L, and T304I.

Publication: Chatterjee S, Bhattacharya M, Dhama K, Lee SS, Chakraborty C (2023) Resistance to nirmatrelvir due to mutations in the Mpro in the subvariants of SARS-CoV-2 Omicron: another concern? Molecular Therapy - Nucleic Acids 32 (13) 263-266 doi:10.1016/j.omtn.2023.03.013 **IF: 8.8 (More than 1 citations)**

1.10. RBD mutation R346X provide an additional fitness to the "variant soup," including offspring of BQ and XBB of SARS-CoV-2 Omicron for the antibody resistance

A newly discovered spike mutation of R346X of SARS-CoV-2, primarily R346T, is found in the offspring of BQ and XBB of SARS-CoV-2 Omicron, especially "variant soup." The mutation is located in the spike receptor-binding domain (RBD) region, and it might provide additional fitness to the offspring of Omicron.

Publication: . Chatterjee S, Bhattacharya M, Dhama K, Lee SS, Chakraborty C (2023) Can the RBD mutation R346X provide an additional fitness to the "variant soup," including offspring of BQ and XBB of SARS-CoV-2 Omicron for the antibody resistance? Molecular Therapy - Nucleic Acids 32:61-63 doi:10.1016/j.omtn.2023.02.030 **IF: 8.8** (*Corresponding Author) **(More than 2 citations)**

2.1. miRNA in Diseases: miRNA in Insulin Signalling Pathway and Insulin Resistance

The work discusses miRNAs that regulate the significant protein cascades in the insulin signaling pathway and insulin resistance. It illustrates the influence of miRNAs in the beta (β) cell development and secretion of insulin. It depicts a model which describes the role of miRNAs in various important protein cascades for insulin signalings like IGF-1 and its IGF1R receptor, IRS (proteins PI3K (phosphatidylinositol 3-kinase),(PKB) protein kinase B/ Akt, and GLUT4 (glucose transporter 4). The model also describes Obesity, hyperlipidemia, and insulin resistance that are significantly associated with T2D and numerous miRNAs.

Publication: Chakraboty C#*, Doss CGP, Bandyopadhyay S# and Agoramoorthy G (2014) Influence of miRNA in insulin signaling pathway and insulin resistance: Micro-molecules with a major role in type-2 diabetes. **Wiley Interdisciplinary Reviews-RNA** 5:697-712 (*Corresponding Author) **IF: 7.3** [https://pubmed.ncbi.nlm.nih.gov/24944010/] **(More than 241 citations)**

2.2. microRNA in Diseases: Mutation in Human AGO2 and the Stability of the miRNA-mRNA Complex

This work demonstrated the features of the interaction of different atoms during the interaction between hAGO2 (human AGO2 protein complex) and miR-20a. It also explains conformational changes in the hAGO2 during complex formation with miR-20ain the native and mutant state. The conformational changes were demonstrated through MDs simulation. RMSD plotted the nucleic acid atomic positions for wild-type miRNA, one and two mutant places in the miRNA. It shows a similar kind of pattern of the fluctuations. However, the changes stabilize after 2 ns

around 0.27 nm. AGO2 protein and its Cα atom illustrated the complex with wild and two mutant positions in the mutation duplex. It shows a stable RMSD value after 20 ns, with a range between the two points of 0.14 nm and 0.21 nm.

Publication: Mallick B, Sharma AR, Lee SS*, **Chakraborty C***. (2019) Understanding the molecular interaction of human Argonaute-2 and miR-20a complex: a molecular dynamics approach. **Journal of Cellular Biochemistry** 120(12):19915–19924. (*Corresponding Author) **IF: 4.0** [https://pubmed.ncbi.nlm.nih.gov/31318096/] **(More than 9 citations)**

2.3. Differential gene expression and lncRNA: gene expression and transcriptome profiling of COVID-19

The study illustrated the (differential gene expression) DEGs in mild and severe (COVID-19 patients) compared to healthy controls. The analysis was performed using the human lncRNA V5 microarray GSE164805 dataset, which is a GEO dataset. It observed significant 29 protein-coding DEGs along with six lncRNAs (DLEU2, TALAM1, and CASC18, UICLM, GNAS, and SNHG20). Finally, the protein-coding DEG-lncRNA network was analyzed. The lncRNAs might act as next-generation biomarkers for COVID-19 patients. All these mapped regulatory genes were linked with immune elements and might be associated with the protective immunity against the virus.

Publication: Chakraborty C*, Sharma AR, Bhattacharya M, Zayed H and Lee SS* (2021) Understanding gene expression and transcriptome profiling of COVID-19: An initiative towards the mapping of protective immunity genes against SARS-CoV-2 infection. **Frontiers in Immunology** 12:724936. doi: 10.3389/fimmu.2021.724936 (*Corresponding Author) **IF: 7.3** [https://pubmed.ncbi.nlm.nih.gov/34975833/] **(More than 14 citations)**

3.1.Vaccine construct development: Multiepitopic peptide vaccine against SARS-COV-2

Here, a peptide-based multi-epitope next-generation COVID-19 vaccinewas designed. It was the first immunoinformatics-based multi-epitope vaccine against SARS CoV-2. We identified T-cell and B-cell epitopes, and finally, common T-cell and B-cell epitopes were identified. They find out the highly antigenic epitopes, and vaccine construct was developed using vaccine construct was with (EAAAK)3 linker peptide [The piece of work was highlighted in another paper PMID: 34276266].

Publication: Bhattacharya M, Sharma AR, Patra P, Ghosh G, Sharma G, Patra BC, Lee SS*, **Chakraborty C*** (2020) Development of epitope-based peptide vaccine against novel Coronavirus 2019 (SARS-COV-2): Immunoinformatics approach. **Journal of Medical Virology** 92(6):618-631.doi:10.1002/jmv.25736 (*Corresponding Author) **IF: 12.7** [https://pubmed.ncbi.nlm.nih.gov/32108359/] **(More than 377 citations)**

3.2. Vaccine Construct Development: Vaccine Candidate Using Alternative Epitopes Against Wuhan and All Significant Mutant Variants of SARS-Cov-2: A Next-Generation Candidate Considering Significant Mutations

The research illustrates a next-generation vaccine design using multi-epitope peptides from four SARS CoV-2 strains (Wuhan variant, B.1.1.28, B.1.351, and B.1.1.7). The vaccine construct was developed using highly antigenic epitopes, which are used as alternative epitopes. The vaccine construct's safety parameters and physicochemical properties were assessed through

immunoinformatics methods. This peptide vaccine construct can boost immunity against most of the significant variants. It is the first immunoinformatics-based vaccine construct that uses alternative epitopes from SARS CoV-2 variants. [The work was highlighted in another paper PMID: 34276266].

Publication: Bhattacharya M, Sharma AR, Ghosh P, Lee SS*, **Chakraborty C*(**2021) A next-generation vaccine candidate using alternative epitopes to protect against Wuhan and all significant mutant variants of SARS-CoV-2: an Immunoinformatics approach. **Aging and Disease** doi: 10.14336/AD.2021.0518 (*Corresponding Author) **IF: 7.4**
[http://www.aginganddisease.org/EN/10.14336/AD.2021.0518] **(More than 19 citations)**

3.3. Vaccine Construct Development whole genome encoded proteins: A novel multi-epitopic peptide-based potential vaccine candidate against monkeypox virus through screening its whole genome encoded proteins

The research demonstrates the development of a novel multi-epitopic peptide-based potential vaccine candidate using an immunoinformatics approach against the monkeypox virus. A whole genome- screening was performed of 176 encoded proteins of MPXV, and the highest antigenic epitopes were used to design the vaccine candidate. Finally, the vaccine was characterized through bioinformatics to understand the physicochemical properties, non-allergenicity, antigenicity, and binding affinity to immune receptors (TLR4/MD2-complex). The designed vaccine has shown the required effectiveness against MPXV without any side effects.

Publication: Bhattacharya M, Chatterjee C, Nag S, Dhama K, **Chakraborty C*** (2022) Designing, characterization, and immune stimulation of a novel multi-epitopic peptide-based potential vaccine candidate against monkeypox virus through screening its whole genome encoded proteins: An immunoinformatics approach. **Travel Medicine and Infectious Disease** 50:102481 doi: 10.1016/j.tmaid.2022.102481 **IF: 12.0** (*Corresponding Author)
[https://pubmed.ncbi.nlm.nih.gov/36265732/]
(More than 13 citations)

3.4. AI-enabled mutation-proof, next-generation vaccine development: A novel mutation-proof, next-generation vaccine to fight against upcoming SARS-CoV-2 variants and subvariants, designed through AI enabled approaches

It was the first AI-based vaccine construct. The study selects nine mutations from 835 RBD mutations AI-enabled, the top-ranked antigenic selection approaches. We selected twelve common antigenic B and T cell epitopes (CTL and HTL) containing the nine RBD mutations and joined them with the adjuvants, PADRE sequence, and suitable linkers. The constructs' binding affinity was confirmed through docking with TLR4/MD2 complex and showed significant binding free energy (-96.67 kcal mol-1) with positive binding affinity. Similarly, the calculated eigenvalue (2.428517e-05) from the NMA of the complex reveals proper molecular motion and superior residues' flexibility. Immune simulation shows that the candidate can induce a robust immune response.

Publication: Bhattacharya M, Alshammari A, Alharbi M, Dhama K, Lee SS, **Chakraborty C.** (2023) A novel mutation-proof, next-generation vaccine to fight against upcoming SARS-CoV-2 variants and subvariants, designed through AI enabled approaches and tools, along with the

machine learning based immune simulation: A vaccine breakthrough. **International Journal of Biological** 242(Pt 2):124893.
[https://pubmed.ncbi.nlm.nih.gov/35952818/]**IF: 8.2 (More than 1 citations)**

3.5. A next-generation vaccine construct for *H. pylori*: A novel multi-epitopic peptide vaccine candidate against Helicobacter pylori through in-silico

Helicobacter pylori (H. pylori) creates patients' ulcers. The study developed a novel vaccine construct for H. pylori using B and T-cell epitopes from four target antigenic proteins (HpaA, FlaA, FlaB, and Omp18). It informed the induction of possible immune responses using advanced immunoinformatics approaches. An adjuvant (50S ribosomal protein L7/L12) with a suitable linker at the N-terminus side of the vaccine sequence was used to boost the immune system. The study uses protein-protein docking between human TLR5 and vaccine construct to understand the way of inductive signaling that leads to immune response. The molecular docking complex's calculated negative score (- 151.4, + / - 8.7) signifies the best binding interface. Molecular dynamics simulation studies confirmed the proper docking between TLR5 and the vaccine candidate.
Publication: Ghosh P, Bhakta S, Bhattacharya M, SharmaAR,, Sharma G, Lee SS, **Chakraborty C***(2021) A novel multi-epitopic peptide vaccine candidate against *Helicobacter pylori*: In-silico identification, design, cloning and validation through molecular dynamics. **International Journal of Peptide Research and Therapeutics** : 27(2):1149-1166. doi: 10.1007/s10989-020-10157-w.(*Corresponding Author)**IF: 2.5**
[https://pubmed.ncbi.nlm.nih.gov/33495694/]/]**(More than 37 citations)**

OTHER SIGNIFICANT RESEARCH CONTRIBUTIONS

Nominee's other research contributions are as follows:

1. Diabetes

Diabetic cases are increasing at an alarming rate throughout the world. It has been noted that the situation is worst in China and India (Chakraborty and Das, 2016). Insulin resistance is one of the leading causes of diabetes, and that is also increasing quickly worldwide. It was reviewed insulin resistance's biochemical and molecular basis (Chakraborty, 2006).In this direction, a significant contribution was made in analyzing the structure-based computational analysis of several signaling cascades of the insulin signaling pathway, type-2 diabetes drug target DPP-4 and its interaction with anti-hyperglycemic drugs (such as 'Sitagliptin' and 'Diprotin –A'), structure-based computational analysis MODY/ MODY2 (maturity-onset diabetes of the young, type 2), correlation between diabetes and miRNA, etc.

1.1. Structure-based computational analysis of several signaling cascades of the insulin signaling pathway

It has been analyzed the phylogenetic analysis of insulin from different animal families (Chakraborty et al. .2012), the evolutionary relationship of the insulin receptor substrate (IRS) family (Chakraborty et al. .2011a), structural topology mapping of IRS family cascades (Chakraborty et al. .2013a), profiling of phosphatidylinositol 3-kinase (PI3K) proteins (Chakraborty et al.2015a) and topology mapping of insulin-regulated glucose transporter GLUT4 (Chakraborty et al.2013b). It was performed the landscape mapping of functional proteins in insulin signal transduction and insulin resistance (Chakraborty et al.2011b) to understand protein-protein interaction in the insulin signaling pathway.

1.2. Structure-based computational analysis MODY /MODY 2 (maturity-onset diabetes of the young, type 2)

It was investigated maturity-onset diabetes of the young (MODY). Genomic roadmap, molecular phylogenetics, and the association between the MODY cascades were analyzed (Chakraborty et al.2015b). Finally, the structure-based computational analysis revealed the deleterious missense mutations on MODY 2.

1.3.Type-2 diabetes drug-target DPP-4 and its interaction with anti-hyperglycemic drugs (such as 'Sitagliptin' and 'Diprotin –A')

Type-2 diabetes(T2D) drug target DPP-4 and its interaction were studied with anti-hyperglycemic medications (such as 'Sitagliptin' and 'Diprotin –A') (Chakraborty et al.2014), and its interaction and micro-environment were evaluated (Chakraborty et al.2014).

1.4. Correlation between diabetes and miRNA/ diabetes-associated pancreatic cancer - miRNA

It has been established a fundamental model of the association of miRNA in (1) insulin signaling pathway and insulin resistance and (Chakraborty et al.2014) (2) insulin resistance and diabetes-associated pancreatic cancer (Chakraborty et al.2013) through computational biology.

2. Human CRP (C reactive protein)

The clinician uses C-reactive protein (CRP)as a marker of inflammation in several diseases. Nominee's students and Nominee have examined conserved domains, conserved residues, and surface cavities of C-reactive protein (CRP) (Kumar et al., 2011). Molecular dynamics and interaction properties such as residue-residue interactions, secondary structure, hydrophobic segment distribution, and stabilization centers were also analyzed (Chakraborty and Agrawal, 2013).

3. Cancer

Along with the EGFR kinase domain (Doss et al.2014b), the anticancer activity of quercetin, a flavonoid molecule, was studied extensively, and apoptotic activity of quercetin was found (Sharma et al.,2015). Somatic mutations in exon 20 and exon 9 of the PIK3CA gene in breast tumors were also studied (Sudhakar et al., 2015). Cyclin-dependent kinases (CDKs) are essential for cell cycle progression, and it retains cell proliferation. Irregularity in the cell cycle and uncontrolled cell proliferation is attributed to cancer. CDK4/cyclin D1 pathway plays a significant role in oncogenesis. Nominee's collaborators and Nominee has identified deleterious nsSNPs in the CDK4 gene. Nominee has evaluated the effects of deleterious CDK4 variants on CDK4-Cyclin D1 protein interactions and drug binding. Molecular dynamics (MD) simulations were performed to comprehend deleterious variants and their impact on CDK4-Cyclin D1 complex formation (Nagasundaram et al., 2015).

4. Bone biology

Professor Chakraborty and his collaborators studied WNT and BMP signaling regulation during titanium particle-induced osteolysis in MC3T3 E-1 cells (Nam et al., 2015). The canonical Wnt/β-Catenin signaling pathway is an essential pathway for bone biology. R-Spondin family proteins, the member of the canonical Wnt/β-catenin signaling pathway, were studied through bioinformatics (Sharma et al., 2014).In another work, in Ti particle-induced osteolysis, we

analyzed the secretion of fibroblast-like synoviocytes arbitrated different pro-inflammatory cytokines(IL-6, IL-8, IL-11, IL-1β, and TNF) secretion. It has been found-1β, IL-6, and TNF was found to be significantly higher.

5. ncRNA/ miRNA analysis

miRNA are small noncoding RNA molecule which is associated with different diseases. The miRNA has a therapeutic role (Chakraborty et al., 2017). miRNA is associated with various diseases, such as Cancer (Chakraborty et al.2018), Alzheimer's disease (Gupta et al.2017), and Rheumatoid arthritis (Sharma et al.2018), and has the potential for its treatment. The research group is trying to understand the mechanism and its potential in treatment. Recently it was analyzed the role of circular RNA in different diseases (Sharma et al. 2021 and 2022)

6. Therapeutic discovery

Ebola is a viral disease that primarily occurs in tropical countries (Jagga et al., 2019; Agoramoorthy and Chakraborty, 2014). Dr. Chakraborty and his collaborators identified inhibitors targeting the viral protein 40 of the Ebola virus through virtual screening. These may be a beneficial therapeutic development of ebolavirus (Karthick et al.2016).

7. COVID-19 and Immunoinformatics

Other than the immunoinformatic-based vaccine (multi-epitope-based peptide-based vaccine) against SARS-COV-2 (Bhattacharya et al. 2020a), it has been observed that spike protein (S protein) has several antigenic sites compared to other structural proteins of SARS-CoV-2. They have identified and characterized the T cell and B cell epitopes of this virus's S protein. The identified common epitopes were linked with a linker for the peptide-based vaccine designed against SARS-CoV-2 (Bhattacharya et al. 2020a). The in silico cloning, validation, and molecular dynamics simulation were performed in of the vaccine candidate and TLR docked complex (Bhattacharya et al. 2020b).

It has been evaluated other human coronaviruses to map protease recognition sites and understand the different antigenic variations of the spike protein. We have also analyzed the clinical trial's current status (Phase-I, II, III) of the different vaccine candidates (Chakraborty et al. 2021a). Finally, the human coronaviruses were grouped through molecular phylogenetics (Chakraborty et al.2021b). At the same time, It has been analyzed various SARS-CoV-2 protein drug targets (Chakraborty et al.2021C). The interaction between the S protein of SARS-CoV-2 protein and hACE2 was analyzed (Chakraborty et al., 2021d).

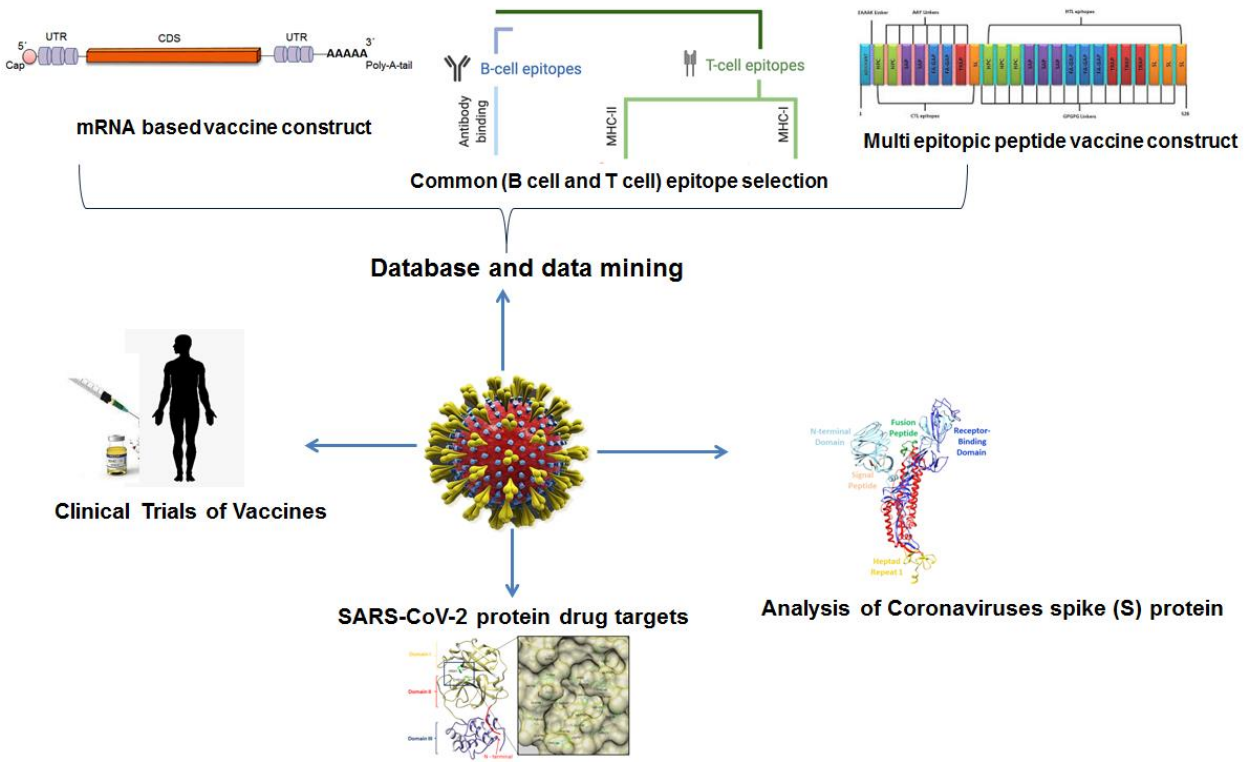

Fig.3. This figure describes our COVID-19 related research work

Along with the mutational landscape of the emerging SARS-CoV-2 variants (Chakraborty et al.2021e), they have recently found that the combination changes the variants in different countries throughout the world. It was noted that the dominancy of the delta variant was pointed out around the globe (Chakraborty et al.2021f).
Moreover, a study was performed by us to determine the DEGs in mild and severe COVID-19 patients versus healthy controls using the human lncRNA V5 microarray GEO dataset (GSE164805 dataset). The analysis highlighted the most significant 29 protein-coding DEGs and six lncRNAs (TALAM1, DLEU2, and UICLM CASC18, SNHG20, and GNAS) involved in the protein-coding DEG-lncRNA network; which might serve as potential biomarkers for COVID-19 patients. At the same time,these mapped regulatory genes were linked with immune elements involved in protective immunity against SARS-CoV-2 (Chakraborty et al.2021g).

8. Development of in silico based other vaccine candidates

Dr Chakraborty and his collaborator have also designed and developed an in-silico vaccine candidate for Aeromonas hydrophila (Bhattacharya et al. 2020c), which is a highly pathogenic bacteria in Prawn and fish culture system. At the same time, the novel epitope candidates were identified from prostate antigen, and a novel vaccine contract against prostate cancer was developed. (Patra,2020).

Conclusion

They have developed the immunoinformatic-based vaccine candidate (multi-epitope-based peptide-based vaccine) against SARS-COV-2. It is the first immunoinformatic-based vaccine candidate (Bhattacharya et al. 2020a). This work has been a well-cited article in Google Scholar within a year (citation index: 301). They have applied for a Korean patent for this innovative approach (Patent application no. 10-2020-0050552 Reference number: P200860). At the same time, the patent was also applied for the peptide vaccine contract against SARS CoV-2. Korean Patent application no. 10-2020-0172923; Reference number: P202300). Moreover, they applied patent for the novel epitope candidates identified from prostate antigen protein (Patent application no. 10-2020-0172924 Reference number: P202350).

Finally, Dr Chakraborty published more than 281 SCI/SCIE and Scopus index articles. **My Research Matrix** is following:

Number of publication: SCIE& Scopus indexed Publications: 281; Book Chapters: 09
Citation in Google Scholar: h-index: **53**; **i10 index**: **146**; **Citation: 8889; 7 Papers with more than 200 citations (i200 index: 7) and 19 Papers with more than 100 citations(i100 index: 19)**
Citation in Scopus: Scopus h-index: **44 Citation: 6396**
Cumulative SCI Impact Factor: 1868.166 Average SCIE Impact Factor:6.62;
Technology developed: 12 ; Patent (Granted):1 Patent (applied): 7
Single Author (SCI & Scopus indexed): 4; First Author (SCI & Scopus indexed): 105;
Corresponding Author (SCI & Scopus indexed):130 (Corresponding since 2003);
PhD guided:03 (Degree awarded);Invited talks: 19; Research Award received: 10

They are looking to contribute more to viral antigenic proteins and cancer antigenic protein research using the Artificial Intelligent-Machine **Learning- Deep learning (AI-ML-DL) approaches and immunoinformatics t**o identify the antigenic peptides from different viruses and cancers to develop a diffident vaccine candidate or unfold the antigen processing to understand the protective immunity against the deadly diseases. They are also planning to use quantum computation-based approaches, such as **Quantum Artificial Intelligent-Machine Learning- Deep learning (AI-ML-DL)** approaches to understand different diseases mechanism and related areas shortly.

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