**Dr. Arindam Talukdar (Nomination No: No:2023/RA-95)**

Senior Principal Scientist, CSIR-Indian Institute of Chemical Biology (IICB), Kolkata

**Signed details of the excellence in research work for which the Sun Pharma Research Award is claimed**

I joined CSIR-Indian Institute of Chemical Biology (IICB) in January 2013 as a Senior Scientist. Recently I have been promoted to Senior Principal Scientist with merit. The following are the major outputs/outcomes of our research group from CSIR_IICB:

i. Advancement of the fundamental concept of medicinal chemistry drug discovery.
ii. Seminal contribution to the field of medicinal chemistry in general.
iii. Empowering and training PhD and Master's students in drug discovery concepts and strategies, which will foresee the advancement of Indian drug discovery research in coming years.
iv. Providing a conceptual drug discovery model with the help of Editorial, Persepectives and Review articles for the medicinal chemistry community for the future generation of the potential drug candidate.
v. Conducting workshops on medicinal chemistry concepts for students (I have conducted four such workshops with international speakers and hands-on training for students across India free of any charges).
vi. Publishing our work in high-impact journals for recognition of Indian Medicinal Chemistry research.
vii. Patenting our work for possible commercialization.

**Contribution towards the Discovery and Development of Selective TLR9 and dual TLR7 and TLR9 Antagonists for autoimmune diseases at CSIR-IICB**

**At CSIR-IICB, I have developed state-of-te-art facility for TLR7/TLR9 Antagonist Drug Development platform, which until now yielded**

| Publications | Patents | Book Chapter |
|---|---|---|
| **Total = 9**<br>Journal of Medicinal Chemistry = 4<br>European Journal of Medicinal Chemistry = 3<br>Molecules = 1<br>ChemMedChem = 1 | **Total = 2**<br>Granted in India, USA, Australia, Europe | **Total = 1**<br>Royal Society of Chemistry |

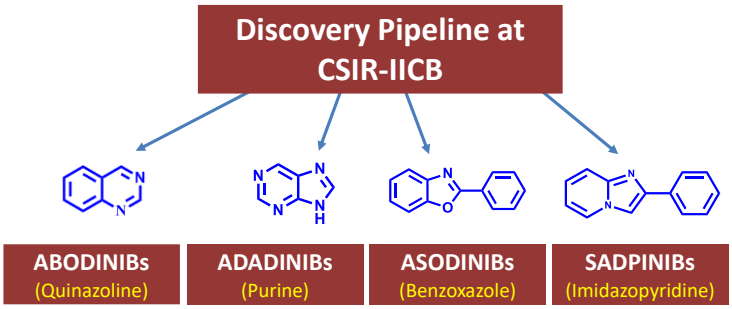
## I. Probing Endosomal Toll-like Receptors (TLRs)

**Introduction to endosomal TLRs:** The human innate immune system is the first line of defense against the invasion of pathogenic microorganisms. Toll-like receptors (TLRs), mostly expressed on antigen-presenting cells such as dendritic cells, are germline-encoded pattern recognition molecules that play key roles in innate immunity by regulating inflammation. Among the family of TLRs, TLR3, TLR7, TLR8, and TLR9 have been identified in humans that are located inside the endosomal compartments (pH = 4.5−6.5) of the immune cells and they recognize nucleic acids of both pathogenic origin and self-origin. In humans, TLR7 and TLR9 are expressed selectively in plasmacytoid dendritic cells (pDCs) and B lymphocytes. Upon activation, they drive type I interferon (IFN) production from pDCs. TLR activation is one of the initial defensive mechanisms utilized by the host to accumulate innate and subsequent adaptive immunity to fight invading pathogens. However, when self-origin RNA or DNA molecules get access to endosomes and aberrantly activate endosomal TLR7/8/9, it initiates autoreactive inflammation in different autoimmune diseases such

as systemic lupus erythematosus (SLE), psoriasis, Sjögren's syndrome and systemic sclerosis. The role of TLR7/9 is well established and can serve as an ideal therapeutic target for novel drug discovery, leading to the amelioration of these diseases. Both TLR7 and TLR9 are structurally similar to each other and initiate common downstream signaling upon activation. This results in the recruitment of the transcription factors NFKB and IRF7, leading to the induction of inflammatory cytokines as well as type I IFNs.

**Discovery and Development of dual and selective TLR7 and TLR9 Antagonists at CSIR-IICB.** Exploration of potent and selective small-molecule TLR7 and TLR9 antagonists as therapeutic agents in several clinical contexts is of great interest, although many candidates are at different stages of a clinical trial as of now none of them are available for clinical use. Previously reported efforts in this context were mainly random in the *absence of the human crystal structure of TLR7 and TLR9*. Among them many candidates are oligonucleotides. Small molecule candidates are always favorable for the well-known reason as oligonucleotides suffer from stability issues, poor pharmacokinetics and dual agonism-antagonism profile.

*The goal of my lab is to conceptualize, rationally design, development and validation of dual as well as selective antagonists for the nucleic acid-recognizing TLRs (TLR7 and TLR9) for devising novel therapeutic strategies in relevant clinical contexts. We have an exhaustive pipeline consisting of molecules from* ***Purine****,* ***Quinazoline****,* ***Benzoxazole*** *and* ***Imidazopyridines****. This platform was established by applying various rational design strategies described below.* ***Till now the work resulted in two GRANTED patents (WO/2019/092739-*** *US20200347062B2-Grant Date: 09.11.2021****; WO2017/163264A1- US10662177B2*** *Grant Date: 26.05.2020****) and many publications in reputed medicinal chemistry journals.***



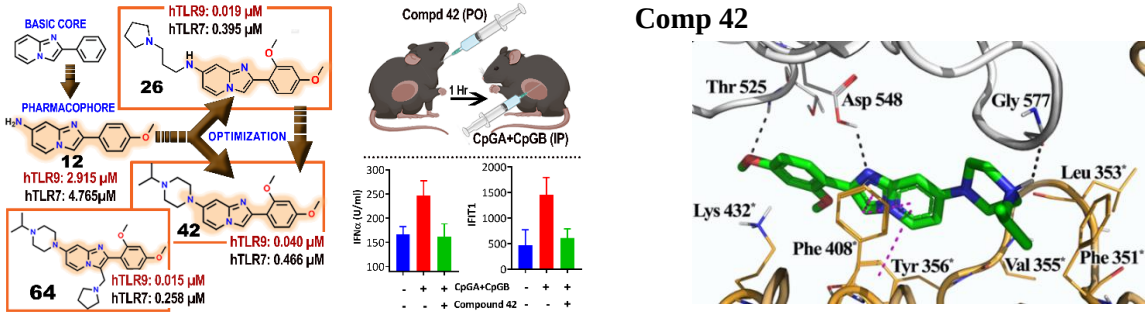

My lab is involved in the conceptualization, design and development of dual TLR7 and TLR9 antagonists or selective TLR9 antagonists (with a selectivity profile of 50 to 500-fold against TLR7) mainly by employing different drug discovery strategies as described below. These molecules were selective against other endosomal TLR8 and a surface TLR4.

## CONCEPTUALIZATION AND DRUG DISCOVERY STRATEGIES EMPLOYED:

**1) Strategic Development of New Chemotypes**
**2) Switching agonist to antagonist structure through '*single-point change*'**
**3) Lead Optimization Strategy**
**4) Activity-Based Design and Development**
**5) Design facilitated by Universal Binding model and ligan-receptor interactions analysis.**
**6) Optimization of Existing Scaffolds**
**7) Medicinal Chemistry Strategy to Mitigate hERG Liability.**
**8) Perspectives, Editorial and Review Articles for the Medicinal Research Community.**
**9) Book Chapter titled Small Molecule Modulators of Endo-lysosomal Toll-like Receptors.**

## DIFFERENT STRATEGIES EMPLOYED FOR DRUG DISCOVERY:

**1) Strategic Development of New Chemotypes.** In the present study, we report the development of a new chemotype "imidazopyridine" as dual TLR7/TLR9 antagonists. The exploration put forth an interesting medicinal chemistry approach starting from imidazopyridine as a basic molecular framework and deducing the chemical spaces through sequentially incorporating relevant structural subunits to identify minimal pharmacophoric features, thereby sculpting the structure−activity relationship (SAR). We identified the structural subunits required for exhibiting selective TLR9 antagonism as well as dual TLR7/9 antagonism. The hit molecules depicted excellent selectivity against TLR8. The optimization provided potential lead molecules with favorable *in vitro* pharmacokinetic parameters with *in vivo* TLR9 and TLR7 antagonism efficacy, depicting therapeutic potential. Modern drug discovery strategies such as high-throughput screening to identify new chemotypes are often out of the reach of academics. Our strategy described herein can be considered as a template for conceptually developing basic chemotypes into a possible drug candidate and can be employed in the academic setup.




Development, Optimization, and In Vivo Validation of New Imidazopyridine Chemotypes as Dual TLR7/TLR9 Antagonists through Activity-Directed Sequential Incorporation of Relevant Structural Subunits. Das N, Bandopadhyay P, Roy S, Sinha BP, Dastidar, UG, Rehman O, pal S, Ganguly D, **Arindam Talukdar** ***.** **Journal of Medicinal Chemistry**, **2022,** *65*, 11607. https://doi.org/10.1021/acs.jmedchem.2c00386

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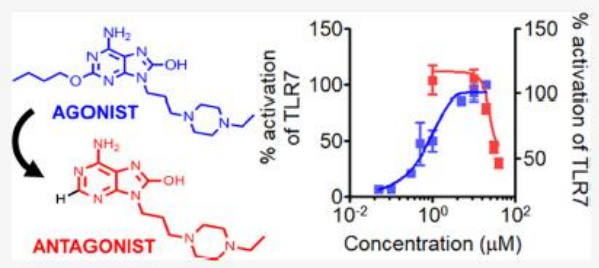
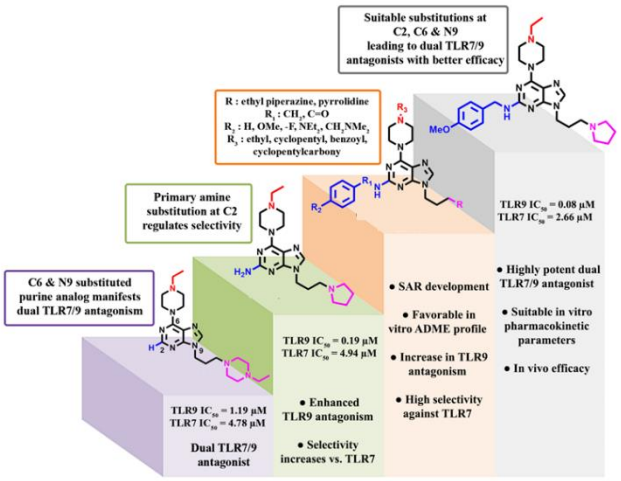
**2) Switching Agonist To Antagonist in Purine Scaffold.** Our approach was to design TLR7/9 antagonist from TLR7 agonist. We hypothesize that both agonist and antagonist of TLR7/9 might bind at a similar site thus, might share similar chemical-structural features for receptor affinity. **Through sequentially eliminating agonistic features, we have mapped the path for transforming agonist to antagonist through a single-point "Chemical Switch".** We have established that a small structural modification 'Chemical Switch' in TLR7 ligand that can lead to a reversal in their functional activity. The removal of the butoxy group at C2 position of the TLR7 purine agonist, transforms the TLR7 agonist into TLR7 antagonist. **This is a seminal contribution to the field of medicinal chemistry in general.**

**Our strategy was included in "Into the Fray! A Beginner's Guide to Medicinal Chemistry'** (https://doi.org/10.1002/cmdc.202000929).



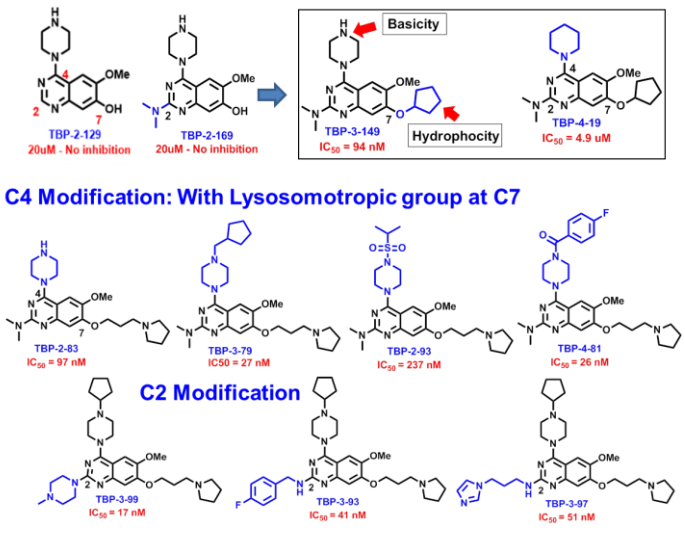

A Chemical Switch for Transforming a Purine Agonist for Toll-like Receptor 7 to a Clinically Relevant Antagonist. Mukherjee A, Raychaudhuri D, Sinha BP, Kundu B, Mitra M, Paul B, Bandopadhyay P, Ganguly D, **Arindam Talukdar*.** **Journal of Medicinal Chemistry**, **2020**, 63, 4776.

**3) <u>Lead Optimization Toward Dual TLR7/TLR9 Antagonists</u>**. We illustrate here the importance of C2, C6, and N9 substitutions in the purine scaffold for antagonism to TLR7 and TLR9 through structure−activity relationship studies using cellular reporter assays and functional studies on primary human immune cells. The lead validation through systematically optimizing via in-vitro DMPK, in-vivo pharmacokinetics, in-vitro and in-vivo toxicity assessment, in-house pharmacodynamic mouse model was done. Isothermal titration calorimetry excluded direct TLR ligand−antagonist interactions. In vivo antagonism efficacy against mouse TLR9 and therapeutic efficacy in a preclinical murine model of psoriasis highlighted the potential of the lead candidate as a therapeutic candidate in relevant autoimmune contexts. (***Journal of Medicinal Chemistry***, **2021**, 64, 9279).




Systematic Optimization of Potent and Orally Bioavailable Purine Scaffold as a Dual Inhibitor of Toll-Like Receptors 7 and 9. Kundu B, Raychaudhuri D, Mukherjee A, Sinha BP, Sarkar D, Bandopadhyay P, Pal S, Das N, Dey D, Ramarao K, Nagireddy K, Ganguly D, **<u>Arindam Talukdar*</u>**. **Journal of Medicinal Chemistry**, **2021,** *64*, 9279. https://doi.org/10.1021/acs.jmedchem.1c00532.

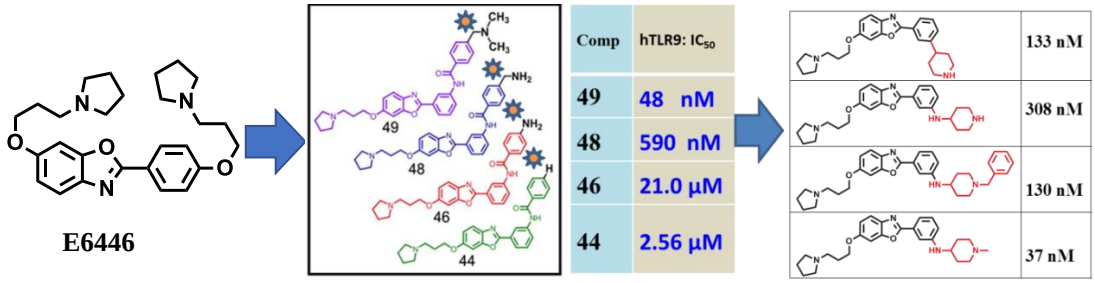
**4) <u>Activity Guided Rational Design: Quinazoline Scaffold</u>.** Through an activity-guided approach, we have identified chemical features in orally bioavailable quinazoline core that are essential for selective hTLR9 inhibition as well as dual TLR7 and TLR9 inhibition. We elucidate the importance of specific physiochemical properties through substitution patterns in quinazoline scaffold to achieve potent hTLR9 inhibition at < 50 nM as well as > 600-fold selectivity against hTLR7.




We found that the substitution patterns at C-2, C-4 and C-7 of the quinazoline ring act in a concerted manner to influence the antagonism. At C-7 position hydrophobicity is important, whereas at the C-4 piperazine nitrogen basicity is important. The C-2 position can accommodate different substitutions, which allows late-stage modifications to counter any issues during validation. We have also optimized the lead candidate with favorable ADME properties along with favorable oral bioavailability, urinary excretion kinetics and in vivo TLR9 antagonism efficacy for one of the representative lead compounds in a clinically relevant rodent model of aberrant TLR9 activation.

Paul B, Rahaman O, Roy S, Pal S, Satish S, Mukherjee A, Ghosh AR, Raychaudhuri D, Bhattacharya R, Goon S, Ganguly D, **<u>Arindam Talukdar*.</u>** Activity-guided Development of Potent and Selective Toll-like Receptor 9 Antagonists. ***European Journal of Medicinal Chemistry***, **2018**, *159*, 187. https://doi.org/10.1016/j.ejmech.2018.09.058.

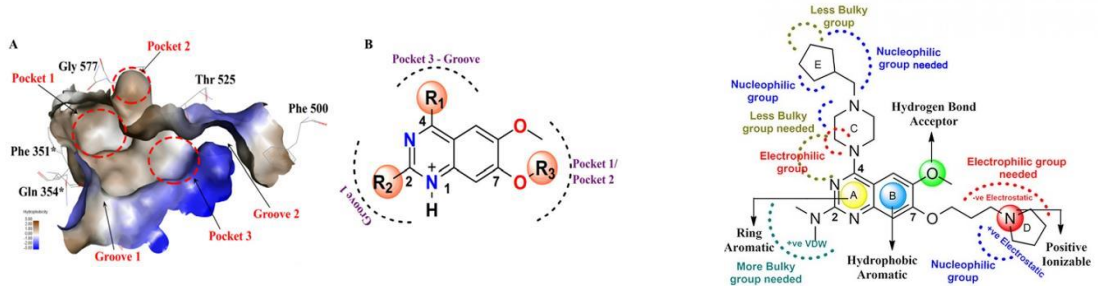
**5) Optimization of Existing Benzoxazole Scaffold.** The study was initiated from a known E6446 hTLR9/hTLR7 antagonist having 2-phenylbenzoxazole core with undesirable molecular flexibility (rotatable bonds). From a drug-designing perspective, our antagonists had lesser molecular flexibility. We provided a correlation between our binding mode hypothesis and hTLR9 antagonistic activity for future rational development.



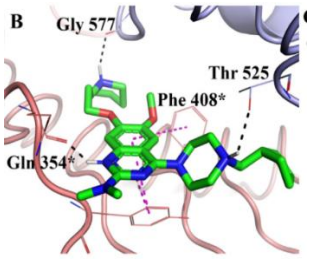

Design and Development of Benzoxazole Derivatives with Toll-like Receptor 9 Antagonism. Roy S, Mukherjee A, Paul B, Rahaman O, Roy S, Maithri G, Ramya B, Pal S, Ganguly D, **Arindam Talukdar***. ***European Journal of Medicinal Chemistry***, **2017**, *134*, 334-347. https://doi.org/10.1016/j.ejmech.2017.03.086.

**6) Design Facilitated by Universal Binding Model.** Due to the unusual topology of the ligand binding surface of TLR9 and TLR7 lacking conventional pockets, the functional mechanism of potential TLR9 antagonism by small molecules is not understood, consequently, small molecule TLR9 antagonists have so far been developed by empirical screening. Our lab has proposed a hypothetical binding model to design TLR9 and TLR7 antagonists. The proposed ligand-receptor interaction could be correlated with TLR7 antagonistic activity thus paving the way for a rational design using varied chemotypes.

**Our hypothetical model was validated through X-ray co-crystal structure of TLR7 published in Nature Comm. by Tojo et. al. doi: https://doi.org/10.1038/s41467-020-19025-z.**

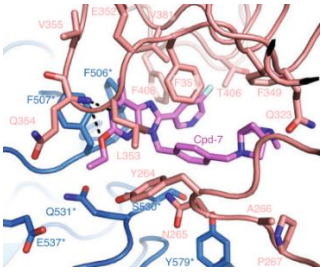



**OUR MODEL: Published: 21 October 2020**




**Our Proposed Binding site analysis.**

**CRYSTAL STRUCTURE: Published: 15 October 2020**




**Actual Binding Site.**

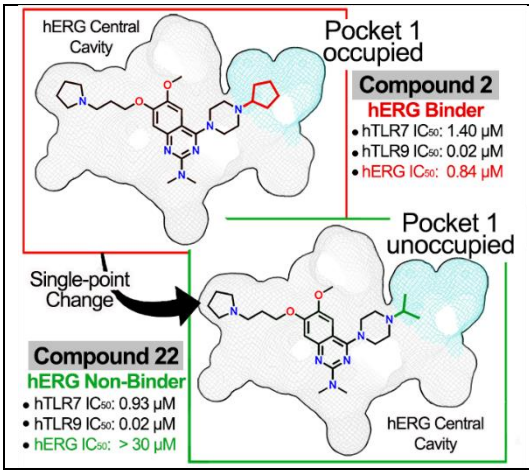
The LRR11-13 and LRR15*-16* in the two sides constitute the antagonist binding site. Thus, residues Phe499, Phe500, Ser523, Gln524, Glu576, Thr525, Gly577, Leu521 in chain A of the first monomer of TRL7 and Tyr264*, Asn265*, Phe349*, Phe351*, Leu353*, Tyr356*, Val381*, Phe408*, Thr406* and Gln354* in chain B of the second monomer of TRL7 can form hydrophobic and hydrogen bond interactions with small-molecule antagonists.

antagonist in the open conformation. The recognition of Cpd-7 is mainly characterized by interactions with hydrophobic residues (Fig. 3e). The 6-methyl adenine ring and 8-fluoropyridine moieties were stacked into a channel formed by F408, F506*, F507* (behind Cpd-7) and F349, F351, L353 (in front of Cpd-7) and V381 (on top of Cpd-7). The N1 atom formed a hydrogen bond with Q354 in the main chain. Moreover, the bulky 9-substituent made additional extensive contacts with Q323, F349, Y264, N265, F351, S530* and Y579*.

i) Synthesis and characterization of new potent TLR7 antagonists based on analysis of the binding mode using biomolecular simulations. Pal S, Paul B, Bandopadhyay P, Preethy N, Sarkar D, Rahaman O, Goon S, Roy S, Ganguly D, **Arindam Talukdar A *.** ***European Journal of Medicinal Chemistry***, **2021**, *210*, 112978. https://doi.org/10.1016/j.ejmech.2020.112978.

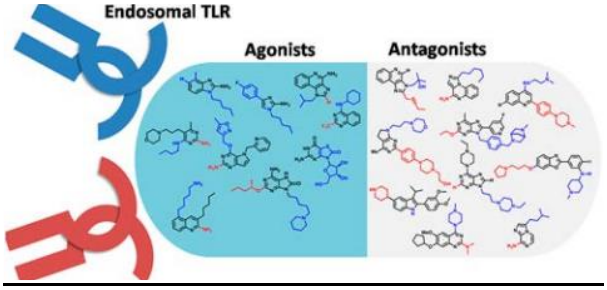
ii) Pal S, Ghosh Dastidar U, Ghosh T, Ganguly D, **Arindam Talukdar*.** Integration of Ligand-Based and Structure-Based Methods for the Design of Small-Molecule TLR7 Antagonists. ***Molecules***, **2022**, *27*, 13, 4026. https://doi.org/10.3390/molecules27134026.

**7) Strategy to Mitigating hERG Liability**. hERG is a primary **ANTI-TARGET in the drug development** process as the K+ channel encoded by hERG plays an important role in cardiac re-polarization. The present study describes a coordinated strategy to integrate the understanding from structure-based protein-ligand interaction to develop **non-hERG binders** with IC50 > 30 µM with retention of TLR7/9 antagonism through a ***single point change*** in the scaffold. This structure-guided strategy can serve as a prototype for abolishing hERG liability during lead optimization. (***ChemMedChem***, **2023**, e202300069. doi: 10.1002/cmdc.202300069).




Mitigating hERG Liability of Toll-Like Receptor 9 and 7 Antagonists through Structure-Based Design. N Das, D Bhattacharya, P Bandopadhyay, UG Dastidar, B Paul, Rahaman O, Hoque I, Patra B, Ganguly D, **Arindam Talukdar*.** ***ChemMedChem***, **2023**, e202300069. doi: 10.1002/cmdc.202300069).

**8) Perspective for Medicinal Chemistry Community.** Recently, we have published a Perspective in J. Med. Chemistry highlighting rational medicinal chemistry approaches to elucidate the structural attributes of small molecules capable of agonism or antagonism or of elegantly switching between the two. The structural evolution of different chemotypes can provide the framework for the future development of endosomal TLR agonists and antagonists.




Structural Evolution and Translational Potential for Agonists and Antagonists of Endosomal Toll-like Receptors. **Arindam Talukdar**,* Ganguly D, Roy S, Das N, Sarkar D. **Journal of Medicinal Chemistry**, **2021,** 64, 12, 8010.

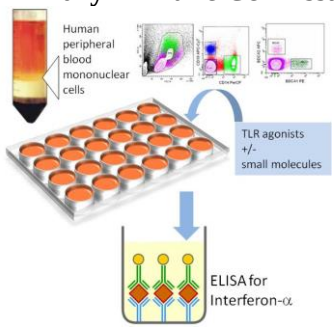
**9) Book Chapter. Small Molecule Modulators of Endo-lysosomal Toll-like Receptors.** This chapter mainly focuses on the endo-lysosomal TLRs. It describes the structural components of TLRs and their modulation through specific ligands with respect to agonists and antagonists. The efforts toward the development of specific small molecule agonists and antagonists for the endo-lysosomal TLRs, which play an important role in different clinical contexts, have been depicted. Agonists have been extensively explored as useful therapeutic agents as well as adjuvants in cancer and infectious diseases. Antagonists have a therapeutic role in suppressing the overactive immune response in chronic inflammatory and autoimmune disorders.

**Protein–Protein Interaction Regulators**. Chapter-13; Small Molecule Modulators of Endo-lysosomal Toll-like Receptors. **Arindam Talukdar**, Ayan Mukherjee, Dipyaman Ganguly. Protein–Protein Interaction Regulators. Royal Society of Chemistry. 2020.

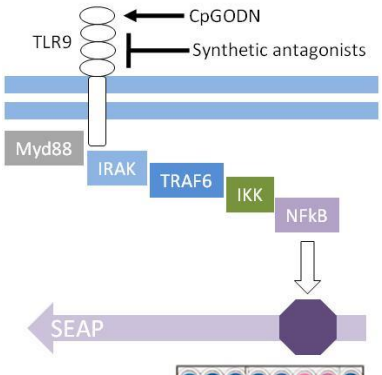
**BRIEF DESCRIPTIONS OF VARIOUS ASSAY PLATFORMS FOR VALIDATION**

In order to find agonistic or antagonistic activity of synthesized molecules, several assay platforms were developed at IICB, Kolkata for screening and validation purposes in TLR4 (for cross selectivity), TLR7, TLR8 and TLR9.

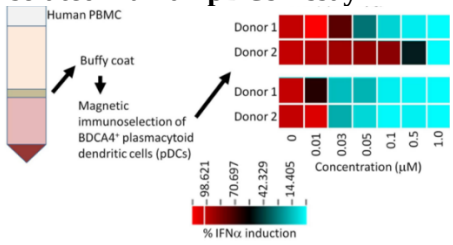
**Primary Immune Cell Assay**




**Reporter Assay**




**Isolated Human pDCs Assay**



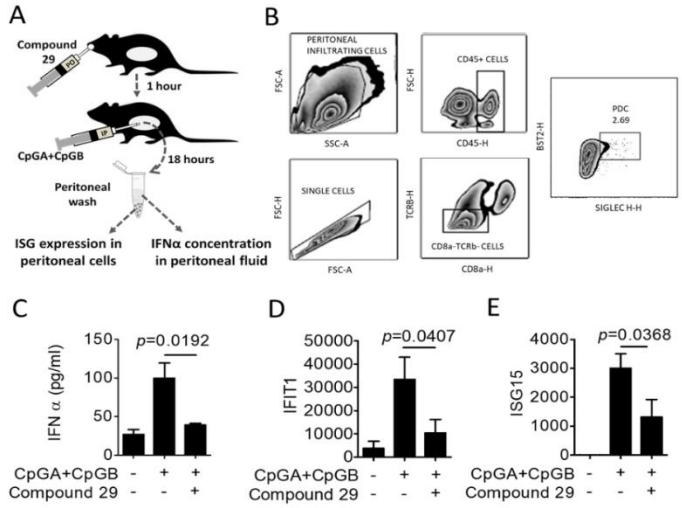

The synthesized compounds were subjected to a three-stage **in-vitro screening** assay.

a) **Medium-throughput Antagonism Assay in Primary hPBMCs.** Primary human PBMCs were isolated from blood taken from healthy individuals. This assay was used for initial screening.

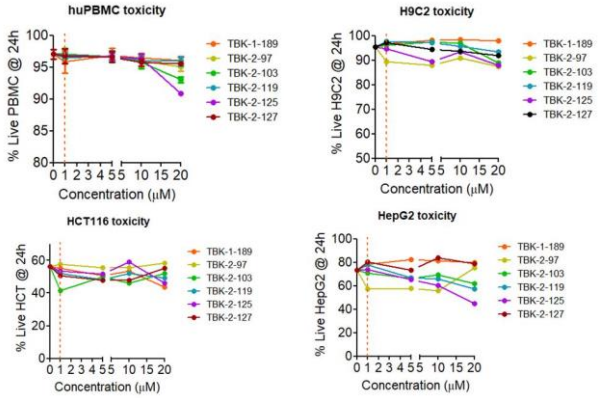
b) **Antagonism in Reporter Cell Line**: The molecules were screened for $IC_{50}$ determination using HEK-Blue™-HTLR7/9/8/4 cells, a HEK293 reporter cell line expressing human TLR7/9/8/4 and a secreted alkaline phosphatase (SEAP).

c) **TLR7/9 Antagonism Assay in isolated Human Plasmacytoid Dendritic Cells (pDCs)**: Human plasmacytoid dendritic cells (pDCs) are enriched in TLR7/9. A primary assay was performed using human pDCs to study the TLR7/9 antagonistic activity for validation.

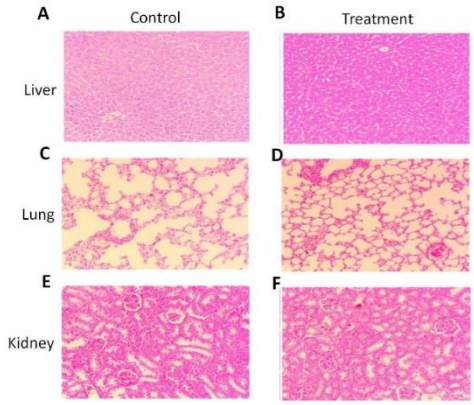
**In-vivo validation in Pharmacodynamic Model**. The model was developed in-house at IICB, Kolkata to check the in-vivo efficacy. Expressions of interferon signature genes (ISGs) in tissues are reliable biomarkers of IFN signaling and are associated with disease activity in clinical contexts. To estimate the in-vivo efficacy of representative TLR9 antagonists, a clinically relevant murine model was developed where mice were administered a mixture of CpGA and CpGB, the bonafide TLR9 agonist, to the peritoneal cavity of mice, which caused immune cell (including pDC) infiltration into the peritoneum. This phenomenon causes the induction of interferon-stimulated genes (ISGs) and IFNα which were analyzed by IFNα ELISA kit and mRNA expression was evaluated by quantitative PCR and flow cytometry.




(A) Oral administration of lead compound at a dose of 10mg/kg body weight of mice was done in the target group of mice 1 hour before i.p. injection of a mixture of CpGA and CpGB. After 18 hours, peritoneal wash was collected. IFNα ELISA was done using the peritoneal fluid, while expression of target genes was monitored in the cellular component. (B) Flow cytometric analysis was done to determine the infiltration of immune cells, especially pDCs into mouse peritoneum. (C) Concentration of IFNα in mice peritoneal fluid w/o administration of compound 1 was measured by IFNα ELISA (2 independent experiments). (D, E) mRNA expression levels of IFIT1(D) and ISG15 (E) in the peritoneal infiltrating cells of mice w/o exposure to compound 29 was quantified by Real-time PCR .




**In-vitro and in-vivo toxicity assessment**. The in-vitro toxicity assessment was done on several cell lines of different tissue origin. Human peripheral blood mononuclear cells (hematopoietic origin), HCT116 (a colon cancer cell line representing gut epithelium of endodermal origin), HepG2 (a hepatocellular carcinoma cell line representing hepatocytes of mesodermal origin), H9C2 (a rat cardiomyoblast cell line representing mesodermal origin) by propidium iodide staining.

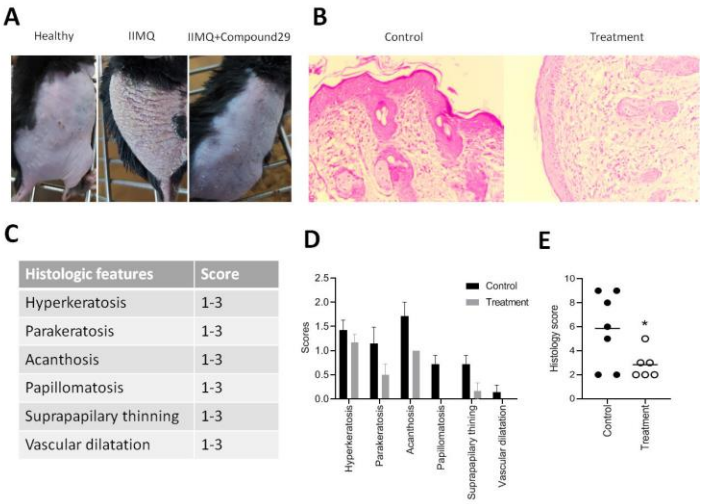



**Short-term visceral toxicity assessment.** Short-term visceral toxicity assessment was also done for lung, kidney and liver cells from sacrificed mice after administration of the lead candidate for 7 days

**In-vitro and in-vivo Pharmacokinetics.** The synthesized molecules were subjected to thorough scrutiny of *in-vitro* pharmacokinetics for assessment of Plasma stability in mice and human, Caco-2 permeability and liver microsomal stability for both mice and human etc. Mice were administered with the desired doses (mg/kg) of synthesized compounds orally and intravenously to checked the parameters ($C_{max}$, $t_{max}$, $t_{1/2}$, AUC, intrinsic clearance; $CL_{int}$, Volume of distribution; $V_{ss}$) and calculation was done for % of oral bio-availability.

| Dose (mg/kg) | Route of administration[a] | $C_{max}$(ng /mL) | $t_{max}$ (h) | $t_{1/2}$ (h) | $AUC_{0\text{-}24h}$ (ng h/mL) | CL (mL/min kg) | Vss(L/kg) | F (%) |
|---|---|---|---|---|---|---|---|---|
| 15 (n=3) | iv | - | - | 0.98 | 50.86 | 3.18 | 4.2 | 70.8 |
| 15 (n=3) | po | 2.6 | 2.0 | 4.6 | 36.06 | - | - | |

**Preclinical Murine Psoriasis Model.** The activity of synthesized compounds finally evaluated in pre-clinical murine psoriasis model developed in-house at IICB, Kolkata. This model bears a strong resemblance to human psoriasis and has been used in multiple studies to explore the pathogenesis of the disease. The model displayed all morphological features associated with psoriasiform inflammation. Histopathologic exploration of psoriatic skin sections from control and treated mice were evaluated and a scoring system of each pathogenic feature such as hyperkeratosis, parakeratosis, acanthosis, papillomatosis, suprapapilary thinning, and vascular dilatation was given to visualize the stark differences between psoriatic and treated mice skin.

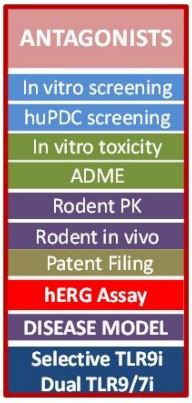



| Histologic features | Score |
|---|---|
| Hyperkeratosis | 1-3 |
| Parakeratosis | 1-3 |
| Acanthosis | 1-3 |
| Papillomatosis | 1-3 |
| Suprapapilary thinning | 1-3 |
| Vascular dilatation | 1-3 |

Efficacy of TLR7 Antagonists in preventing Psoriasis like inflammation in rodent- structure. The ability of our lead compound to significantly reduce disease severity of a TLR7/9 driven autoimmune disease in vivo, could be established.

**COMPOUND PROGRESSION & VALIDATION PROCESS**

**PATENTS GRANTED**





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**Talukdar et al.** (43) **Pub. Date: Mar. 28, 2019**

(54) **BLOCKING TOLL-LIKE RECEPTOR 9 SIGNALING WITH SMALL MOLECULE ANTAGONIST**

(71) Applicant: **Council of Scientific & Industrial Research**, New Delhi (IN)

(72) Inventors: **Arindam Talukdar**, Jadavpur (IN); **Dipyaman Ganguly**, Jadavpur (IN); **Barnali Paul**, Jadavpur (IN); **Ayan Mukherjee**, Jadavpur (IN); **Shounak Roy**, Jadavpur (IN); **Swarnali Roy**, Jadavpur (IN); **Amrit Raj Ghosh**, Jadavpur (IN); **Roopkatha Bhattacharya**, Jadavpur (IN); **Oindrila Rahaman**, Jadavpur (IN); **Biswajit Kundu**, Jadavpur (IN)

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CPC ..... ***C07D 403/12*** (2013.01); ***A61P 37/04*** (2018.01); ***C07D 239/95*** (2013.01); ***C07D 403/14*** (2013.01); ***C07D 401/12*** (2013.01); ***C07D 403/04*** (2013.01)

(57) **ABSTRACT**

The present invention relates to small molecule4-(piperazin-1-yl)quinazolin-2-amino compounds with formula (I) useful for inhibiting signalling by certain toll-like receptors (TLRs), especially TLR9. Toll-like receptors (TLRs) are members of the larger family of evolutionarily conserved pattern recognition receptors which are critical first line of defence for self-nonself discrimination by the host immune response. Aberrant TLR9 activation is implicated in auto-reactive inflammation in different autoimmune diseases. The invention depicts compounds with formula (I), composition and methods can be used in a number of clinical applications, including as pharmaceutical agents and methods for treating conditions involving unwanted immune activity due to TLR9 activation.

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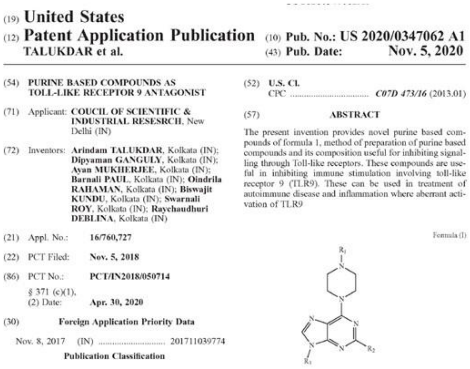
(19) **United States**
(12) **Patent Application Publication** (10) **Pub. No.: US 2020/0347062 A1**
**TALUKDAR et al.** (43) **Pub. Date: Nov. 5, 2020**

(54) **PURINE BASED COMPOUNDS AS TOLL-LIKE RECEPTOR 9 ANTAGONIST**

(71) Applicant: **COUCIL OF SCIENTIFIC & INDUSTRIAL RESESRCH**, New Delhi (IN)

(72) Inventors: **Arindam TALUKDAR**, Kolkata (IN); **Dipyaman GANGULY**, Kolkata (IN); **Ayan MUKHERJEE**, Kolkata (IN); **Barnali PAUL**, Kolkata (IN); **Oindrila RAHAMAN**, Kolkata (IN); **Biswajit KUNDU**, Kolkata (IN); **Swarnali ROY**, Kolkata (IN); **Raychaudhuri DEBLINA**, Kolkata (IN)

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CPC ..... *C07D 473/16* (2013.01)

(57) **ABSTRACT**

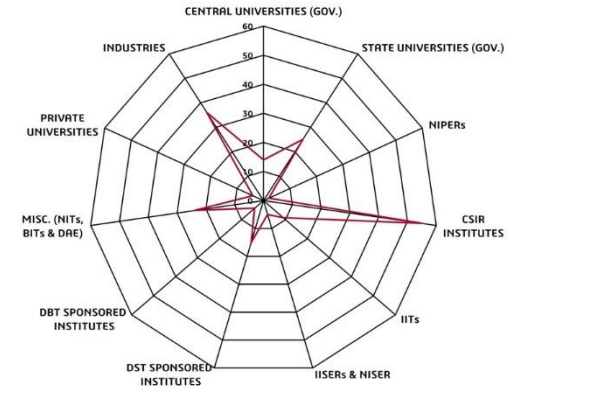
The present invention provides novel purine based compounds of formula 1, method of preparation of purine based compounds and its composition useful for inhibiting signalling through Toll-like receptors. These compounds are useful in inhibiting immune stimulation involving toll-like receptor 9 (TLR9). These can be used in treatment of autoimmune disease and inflammation where aberrant activation of TLR9

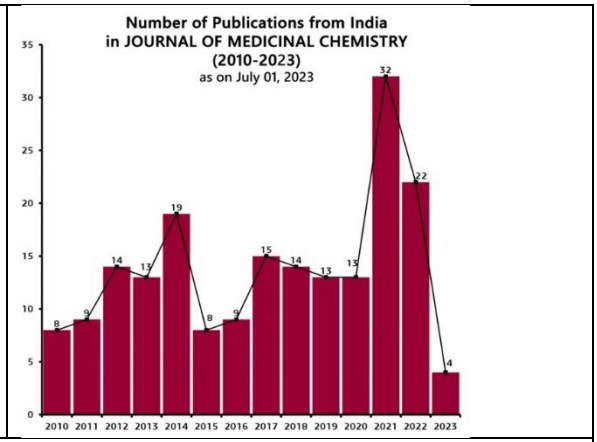
Formula (I)

**US20200347062B2; Grant Date: 09.11.2021**

**EDITORIAL in the Journal of Medicinal Chemistry**

Recently, I wrote An Editorial on Indian Medicinal Chemistry Research scenario titled: **"Catalyzing the Future of Medicinal Chemistry Research in India"**. The Editorial provides a comprehensive look at more than a decade (2010 to midyear of 2023) of medicinal chemistry research in India, focusing on contributions to medicinal chemistry and drug discovery from both Indian academia and industries. The work provides an overview of cutting-edge medicinal chemistry research along with the organic-transformation-based chemical research scenarios in India in the past decade. It also distinguishes areas of research as well as contributions from different federal research institutes, state universities, central universities, and private universities by their geographical locations around India. The paper takes broader stock of the situation by comparing the articles published in the two internationally acclaimed journals in the field, viz. Journal of Medicinal Chemistry and Organic Letters, which highlights the current research trends as well as the thrust needed at the grass-roots level to boost medicinal chemistry and drug discovery research in India. *Finally, we believe that this discussion may create a pathway for policymakers and funding agencies to focus their efforts on motivating lesser inclined institutions as well as provide incentives to the institutions primarily involved in medicinal chemistry research, as they already have built capacity for such research.*

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Dr. Arindam Talukdar, PhD
Senior Principal Scientist
Organic and Medicinal Chemistry Division
CSIR- Indian Institute of Chemical Biology, Kolkata
Email: atalukdar@iicb.res.in: Phone: 9051646141
https://iicb.res.in/faculty/arindam-talukdar