List of top 10 publications in the importance order:

1. Singh R, Chandrashekharappa S, Bodduluri SR, Baby BV, Hegde B, Kotla NG, Hiwale AA, Saiyed T, Patel P, Vijay-Kumar M, Langille MGI, Douglas GM, Cheng X, Rouchka EC, Waigel SJ, Dryden GW, Alatassi H, Zhang H-G, Haribabu B, **Vemula PK,*** Jala VR.*
"Enhancement of the gut barrier integrity by a microbial metabolite through the Nrf2 pathway"
Nature Communications 2019, *10*, 89.

In this publication, 'biomimicry based drug discovery' has been demonstrated. Vemula and his collaborators focused their efforts on identifying microbial metabolites that trigger overexpression of tight junction proteins in gut epithelial cells to restore barrier function. They targeted the aryl hydrocarbon receptor (AhR)/Cyp1A1/Nrf2 pathway and showed mild activation of AhR by a gut microbial metabolite, urolithin-A and its mimics, which restores the gut barrier. However, nature gut metabolite does not have drug-like properties, therefore, through targeted medicinal chemistry approach, synthetic analog has been developed which was far more efficient than natural metabolite. Based on this work, Vemula co-founded a spin-off company, Artus Therapeutics, Inc. Furthermore, Vemula has done three rounds of medicinal chemistry to identify four lead compounds that exhibited optimal safety and toxicity profile in IND-enabling study. Based on this invention, Vemula's team will be filing Investigative New Drug (IND) application to the US-FDA to start the Phase I clinical trials in coming years. If their lead compound show promising results in clinical trials, it will impact >250 millions of IBD patients, worldwide.

In this work, Vemula has conceptualized the idea, and lead entire medicinal chemistry efforts and in vitro studies. His collaborator Dr. Jala lab has tested these compounds in preclinical IBD models.

2. Thorat K, Pandey S, Chandrashekharappa S, Vavilthota N, Hiwale AA, Shah P, Sreekumar S, Upadhyay S, Phuntsok T, Mahato M, Mudnakudu-Nagaraju KK, Sunnapu O, **Vemula PK.***
"Prevention of pesticide-induced neuronal dysfunction and mortality with nucleophilic *poly*-Oxime topical gel"
Science Advances 2018, *4*, eaau1780.

A platform technology with enormous potential to address a major unmet clinical need, developed in Vemula's lab is reported in this paper. This has particular significance for the agricultural farming community in India. The use of organophosphate-based pesticide sprays is widespread and the mainstay of the farming community, which nonetheless constitutes a health hazard for the farmers following inhalation or contact through nasal and dermal routes, respectively. Exposure to pesticides while spraying leads to a plethora of toxic effects, including neuronal toxicity, loss of neuromuscular function, paralysis and death. Furthermore, there is no existing technology to prevent pesticide exposure in farmers. Therefore, to solve this unmet need, Vemula's lab has developed a nucleophilic polymer-based topical hydrogel, which can be applied to the skin like a cream. This cream chemically deactivates pesticides through nucleophile-mediated hydrolysis to prevent pesticide-induced toxicity and mortality, *in vivo*. This topical gel could completely prevent pesticide-exposure.

The entire work has been conceptualized and conceived in Vemula's lab. Based on this work, Vemula co-founded a start-up company, Sepio Health Pvt Ltd., which is going to commercialize this technology.

3. Pandey S,[#] Mahato M,[#] Srinath P, Bhutani U, Goap TJ, Ravipati P, **Vemula PK.***
"Intermittent scavenging of storage lesion from stored red blood cells by electrospun nanofibrous sheets enhances their quality and shelf-life"
Nature Communications 2022, *13*, 7394.

Despite inadequate blood donation, millions of units of blood are being discarded due to the decline of its quality during storage. Typically, stored cells produce various extracellular components known as damage-associated molecular patterns (DAMPs), which damage the blood cells during storage. Typical extracellular components being generated are i) extracellular DNA, ii) nucleosomes, iii) free-iron, iv) free-hemoglobin, v) bioactive lipids such as poly unsaturated fatty acids, and vi) proteins. During the storage, these components interact and damage red blood cells (RBCs). Capturing these DAMPs components without causing damage to the stored blood cells is highly challenging. Therefore, Vemula's group has developed nanofibrous sheets from custom-designed polymers that can capture such damage-causing components and protect RBCs to increase the quality and shelf-life of the blood. These nanofibrous sheets can be made into novel blood bags.

Typically, blood can be stored for maximum for 42 days. However, in clinics, typically less than 21 days stored blood is used for transfusion. However, with this new blood bag technology the quality of 42 days of stored old blood has increased and it is as good as freshly collected blood. Additionally, with this technology, the maximum shelf-life of stored blood has increased by 25%.

The entire work has been conceptualized and conceived in Vemula's lab. Based on this work, Vemula co-founded a start-up company, CaptureBio Pvt Ltd., which is going to commercialize this technology.

4. Gajanayake T, Olariu R, Leclere FM, Dhayani A, Yang Z, Bongoni AK, Banz Y, Constantinescu MA, Karp JM,* **Vemula PK**,* Robert R,* Vogelin E.
"A single localized dose of enzyme-responsive hydrogel improves long-term survival of a vascularized composite allograft".
Science Translational Medicine 2014, *6*, 249ra110.

In this publication, disease/inflammation-responsive biomaterials developed and inflammation-response drug delivery has been demonstrated. This material has shown to prevent the rejection episodes in transplanted organs, and it enabled extension of the lifetime of transplanted grafts (vascularized composite tissue) while eliminating systemic side effects. Typically, post-transplantation of organs, patients need to be on immunosuppressants for their entire life, which leads to global immunosuppression, compromising the ability to fight infections. As a result, these patients suffer from infections that potentially can lead to death. The injectable hydrogels developed by Vemula lab can overcome these limitations and enhance the lifetime of the transplanted organs.

In this publication, it has demonstrated that these injectable hydrogels were shown to release the drugs in response to inflammation, and repeated periodic administration of these gels prevented the rejection of transplanted limbs without causing the global immunosuppression.

In this project, Vemula has conceived the idea of the project and developed hydrogels. Additionally, conceptual demonstration using in vitro assays were done at Vemula's lab. Transplantation surgeries and in vivo efficacy studies were done at collaborators' laboratories.

5. Jain A, Dhiman S, Dhayani A, **Vemula PK,*** George S.*
"Chemical fuel-driven living and transient supramolecular polymerization"
Nature Communications 2019, *10*, 450.

On the contrary to the previous papers, in this work, a fundamental phenomenon has been studied. Self-assembly of biomolecules, typically, bi-directional and dynamic, such as actin self-assembly. Unlike biomolecules, chemical molecules self-assembly is often unidirectional and primarily determined by thermodynamic/kinetic stability. A chemical fuel driven self-assembling system can not only be grown in a controlled manner, but it can also result in precise control over the assembly and disassembly kinetics. In this paper, we clearly showed that once a chemical fuel driven self-assembly is established it can be made receptive to multiple molecular cues such that the inherent growth and decay characteristics are programmed into the ensemble.

Vemula lab has contributed in molecular design and developed multiple cues responsive self-assembled systems.

6. Sasidharan V,[#] Marepally S,[#] Eliott SA, Baid S, Lakshmanan V, Nayyar N, Bansal D, Sanchez-Alvarado A, **Vemula PK,*** Palakodeti D.*
"The miR-124 family of microRNAs critical for regeneration of the brain and visual system in the planarian Schmidtea mediterranea"
Development 2017, *144*, 3211-3223.

Plat worm planaria is one of the most robust animal models for studying regenerative biology. However, the biggest lacune with this model is lack of transgenic planaria. Thus far, it is difficult to deliver nucleic acids into planaria, which is limiting the possibility of developing transgenic model. Therefore, we systematically developed nucleic acid delivering self-assembling systems that could efficiently deliver microRNAs in to full animal. This phenomenon enabled us to identify the role of miR-124 family of microRNAs in regeneration of the brain and eyes. Due to this technology advancement, this paper is considered as one of the highly appreciated publication in the planaria field.

In this work, Vemula lab has designed and developed nucleic acid delivery vehicles, where his collaborator Dr. Palakodeti lab has demonstrated their efficacy in planaria model.

7. Kurbet AS, Hegde S, Bhattacharjee O, Marepally S, **Vemula PK,** Raghavan S*.
"Sterile inflammation enhances ECM degradation in integrin β1 KO embryonic skin"
Cell Reports 2016, *16*, 3334-47.

Dr. Srikala Raghavan lab was investigating the role of sterile inflammation in embryonic skin homeostasis. However, one of the biggest challenge to study this phenomenon was lack of *in utero* specific drug delivery systems. Therefore, Vemula lab has developed novel self-

assembled biomaterials for the localized *in utero* delivery of drugs and biologics for combating sterile inflammation in embryos.

8. Ghate V,* Renjith A,* Badnikar K, Pahal S, Jayadevi SN, Nayak MM, **Vemula PK,*** Subramanyam DN.
"Single step fabrication of hollow Microneedles and an experimental package for controlled drug delivery"
International Journal of Pharmaceutics 2022, *632*, 122546.

This publication describes developing hollow microneedles-based wearable device which can deliver modulated doses of drugs through transdermal route in an on-demand manner. With a specific degree of rotation the dose of the drug could be controlled. It has been demonstrated that such wearable device could use for delivering the drugs, such as insulin to achieve glycemic control in an on-demand manner. In the future, this device will be miniaturised further to enable wearing on wrist.

Vemula lab collaborated with the engineers from Indian Institute of Science to prototype the device, and in Vemula lab both in vitro and in vivo validation has been done.

9. Dhayani A, Bej S, Mudnakudu-Nagaraju KK, Chakraborty S, Srinath P, Kumar AH, PS AM, Khristi A, Ramakrishnan S,* **Vemula PK.***
"An amphiphilic double-brush polymer hydrogel for sustained release of small molecules and biologics: Insulin-delivering hydrogel to control hyperglycemia"
ChemNanoMat 2022, e202200184.

As a part of developing strategies to deliver insulin to control hyperglycemia, insulin-laden injectable hydrogel has been developed. These hydrogel materials are robust and can encapsulate a wide range cargo including small-molecular drugs and biologics as well. Using these novel hydrogel system, sustained release of insulin has been achieved, therefore, number of repeated injection were reduced to achieve better control of hyperglyemia. For example, to achieve 24 hour glycemic control, four repeated injections of conventional insulin formulation is required, whereas same efficacy will be achieved using a single injection of insulin-laden hydrogel, *in vivo*.

10. Rachamalla H, Voshavar C, Arjunan P, Mahalingam G, Chowath R, Banerjee R, **Vemula PK,*** Marepally S.*
"Skin permeable nano-lithocholic-lipidoid efficiently alleviates psoriasis-like chronic skin inflammations"
ACS Applied Materials & Interfaces 2022, *14*,14859-14870.

Long-term application of topical therapeutics for psoriasis has a plethora of side effects. Additionally, skin-permeating agents used in their formulations for deeper dermal delivery damage the skin. To address these limitations, we developed novel lithocholic acid analogues that could form lipid nanoparticles (nano-LCs) spontaneously in the aqueous milieu, permeate through the skin, penetrate the deeper dermal layers, and exert anti-inflammatory effects against psoriasis-like chronic skin inflammations. Nano-LC10 also reduced systemic inflammation, organ toxicity, and also proinflammatory serum cytokine levels. Overall, nano-lithocholic

lipidoid (nano-LC10) can be a potential novel class of therapeutics for topical application in treating psoriasis.