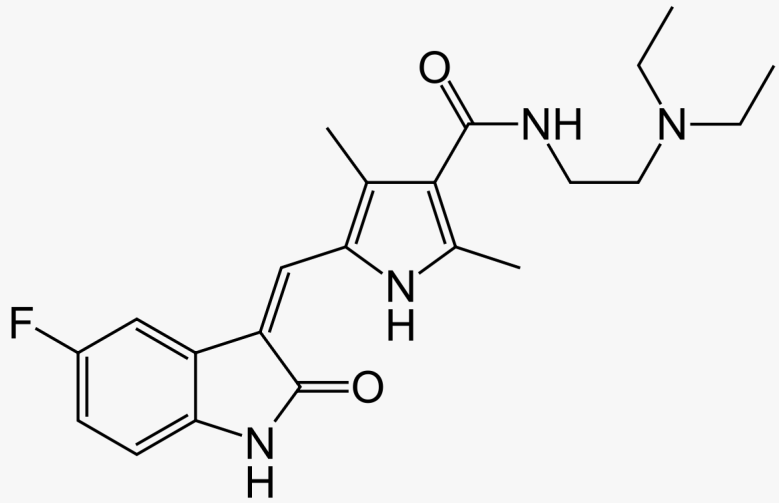
The Fourth Wave of Drug Discovery

VulcanChem welcomes the advent of multispecific drugs that induce proximity to enable targeted cell degradation.



Sunitinib - an example of multispecific drug

PASADENA, CALIFORNIA, UNITED STATES, September 14, 2020 /EINPresswire.com/ -- Dr. Ray Deshaies, senior vice president of global research at Amgen, believes he has identified the “fourth wave” of drug discovery: the advent of multispecific drugs that induce proximity to enable targeted cell degradation. In a paper published earlier on Nat. Rev. Drug Discov., Dr. Deshaies, brilliantly and systematically summarized the current hot topic, multispecific drugs, which represent the fourth revolutionary wave of biopharmaceutical innovation that is now sweeping over the biopharmaceutical industry.

The past 120 years have seen three waves of transformative innovation in the development of drugs: the first wave, namely random screening for active substances from culture broths or biological extracts, which started from the early 20th century and now seldom uses; the second wave, which is rational drug discovery methodology, beginning in the 1970s and now still dominating the drug research and development; the third wave, recombinant protein-based therapeutic agents, starting in the 1980s and still growing fast at present. We are now witnessing the coming of the fourth wave, multispecific drugs.

“In the future, medicines could function very differently than conventional medicines do today. In biopharma pipelines across the industry, we’re seeing more and more multispecific drugs that can form connections with two or more proteins,” said Deshaies. “They include some highly sophisticated structures that function as molecular matchmakers. By inducing proximity between their targets and natural enzymes or even cells, multispecifics can harness the awesome power of biology to go well beyond what conventional drugs can accomplish. This isn’t an incremental improvement in drug design, it’s a sea change.”

What are the major differences between the multispecific drugs and classical drugs? The classical

drugs, including small molecule drugs and macromolecule antibodies, follow the principle of one target and one drug. On the contrary, multispecific drugs work through two or more entities, either limiting drug activity to a specific location or anchoring the target close to an endogenous effector such that allowing the effector to modulate the target. On one end the drug binds to the target to be altered (inhibited, activated, or destroyed) and the other end binds to the cellular effector that acts on the target. Matchmaker multispecific drugs have the potential to target the 85% of proteins currently thought of as "undruggable."

“A lot of people have written reviews of antibody drug conjugates (ADCs), bispecific T cell engagers and PROTACs, but this is something bigger. All of these are different types of multispecifics, and if Amgen’s portfolio is any reflection of the rest of the industry, this is a movement. This is not just a one-off here or there, this is a movement. It’s going to change our whole industry,” asserted Dr. Deshaies.

One example of the multispecific drugs is sunitinib, commercially known as Sutent. Sunitinib is a cancer drug with a specific mechanism of action: by simultaneously blocking several molecular targets (so-called multi-specificity) of essential importance for the onset of cancer it addresses the complexity of tumorigenesis in a very efficient manner. Sunitinib interferes with this logistical feat by blocking one of the receptors responsible for angiogenesis. This receptor, called Flk-1 or VEGFR-2 (vascular endothelial growth factor receptor 2), is expressed by endothelial cells responsible for the formation of new blood vessels. If it is blocked, no new blood vessels can grow around or into the tumor tissue. As a result, the tumor is unable to grow.

VulcanChem welcomes the advent of multispecific drugs that induce proximity to enable targeted cell degradation. The chemists, biologists, and other scientists at VulcanChem supply quality compounds for multispecific drug discovery and research.

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