

# A mystery no longer: Biological Roles for Z-RNA and Z-DNA

*Unlocking the mystery of Z-DNA*

CHARLESTOWN, MA, UNITED STATES, March 14, 2023 /EINPresswire.com/ -- A quote attributed to Yogi Berra makes the observation that "It's tough to make predictions, especially about the future," highlighting the difficulties associated with new scientific discoveries. Notably they are

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Move over Watson-and-Crick. B-DNA is so low energy compared to the other conformations DNA adopts The data suggests that genetic information is encoded not only by sequence, but also by DNA shape”

*Alan Herbert*

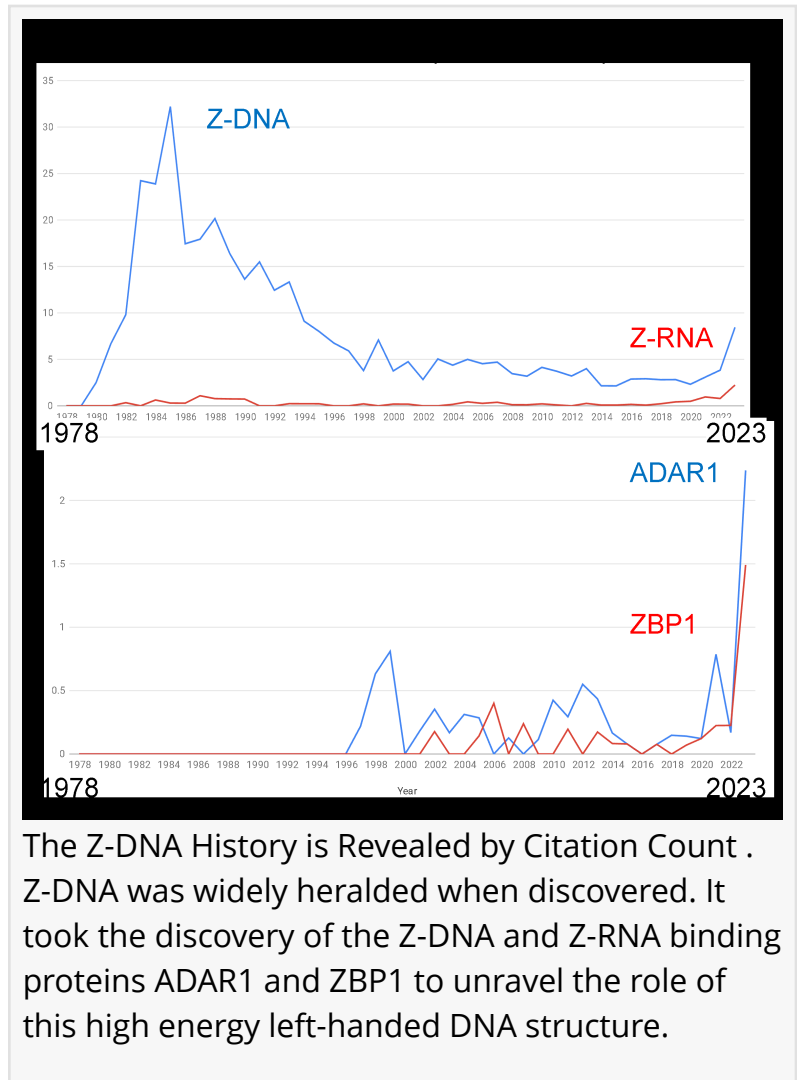
greeted with skepticism and the proverbial “cold-shoulder” in terms of funding from Government agencies and from the community. Even though this phenomenon is well known, the cycle repeats itself again and again. The history of Z-DNA follows this trend. Today a new book has been released that documents the path to the discovery of biological roles for the high energy left-handed Z-DNA and Z-RNA conformations. The various chapters in the book entitled “[Z-DNA: Methods and Protocols](#)” edited by Vinrod Subramani and Kyeong Kim. captures the contributions of many. Dr. Herbert from InsideOutBio captures many of the key discoveries that have turned the field around in his chapter entitled “[Z-DNA and Z-RNA: Methods-Past and](#)

[Future](#)” .

It is now clear that the proteins that recognize Z-DNA and Z-RNA play an important role in protecting against viral infection and in the etiology of auto-inflammatory diseases. The new insights provide a rationale for therapeutics that target cancers able to switch off the immune response.

While the discovery of Z-DNA was greeted with enthusiasm initially, many early postulates about its biology have failed the test of time, both those from proponents who were wildly enthusiastic in enunciating roles that till this day still remain elusive to experimental validation and those from skeptics within the larger community who considered the field a folly, presumably because of the limitations in the methods available at that time. If anything, the biological roles we now know for Z-DNA and Z-RNA were not anticipated by anyone, even when those early predictions are interpreted in the most favorable way possible. The breakthroughs in the field were made using a combination of methods, especially those based on human and mouse genetic approaches informed by the biochemical and biophysical characterization of the Z $\alpha$  family of

proteins. The first success was with the p150 Z $\alpha$  isoform of ADAR1 (adenosine deaminase RNA specific), with insights into the functions of ZBP1 (Z-DNA-binding protein 1) following soon after from the cell death community. Just as the replacement of mechanical clocks by more accurate designs changed expectations about navigation, the discovery of the roles assigned by nature to alternative conformations like Z-DNA has forever altered our view of how the genome operates. We now know that genetic information can be encoded by sequences that can change their conformation under physiological conditions. These elements called [flipons](#) are often composed of repeat sequences that have no inherent information due to their high frequency in the genome. However, when they change shape, they can trigger biological responses. The energy to trigger the flip is generated in genes that are actively transcribed, enabling flipons to change outcomes in a context-specific manner by changing their structure, as described recently.



InsideOutBio is an early-stage biotech company developing therapeutics for the treatment of cancer. The access to the enormous databases created by collaborative international efforts has helped the InsideOutBio scientists make fundamental discoveries such as those reported by Dr. Herbert in the paper. InsideOutBio is privately held. And this research received no external funding.

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