Editorial

CRISPR-Cas Technology: A Role in Transcriptional Recording and Chromatin Remodeling Events

The CRISPR/Cas (Clustered Regularly Interspaced Short Palindromic Repeats/CRISPR associated nucleases) is a widely appreciated genome editing tool and essentially this system is a key component of an acquired immune response mechanism existing in archaea and bacteria [1-11].

In the era of chromatin remodeling, transcriptional event recording and genome editing, CRISPR/Cas tool is widely acknowledged as a precision-targeted genome editing tool to genetically engineer higher organisms with an intended genotypic and phenotypic landscape [3-11].

Recently, diverse modifications of CRISPR-Cas tool in the form of Cas9, Cas12a, Cas1, Cas4 and CasDrop are reported to reduce the chance of off-target action and better precision in the targeted genome [4-11]. At the same time, the use of CRISPR/Cas is highlighted in addition to genome editing, including transcriptional event recording and chromatin remodeling and mechanical fingerprint [4-11].

An elegant paper by Schmidt et al. [8] clearly elucidates the importance of transcriptional recording within Escherichia coli to decipher the complex cellular process. However, the authors address the CRISPR spacer acquisition-mediated recording of transcriptional events by using well designed experimental strategies. In the current perspectives, these tools and evidence of transcriptional recoding will boost to both basic and translational aspects of biology, where a plethora of stimuli change our cellular responses, including transcriptional events and thereafter molecular recording by using synthetic tools like CRISPR editing tools. Furthermore, the author would like to suggest that the existence and need of molecular recorder within a cell can be for both transcriptional and epigenetic events that would be besides earlier reported evidence on the molecular eraser, writer and reader in our genome. On the same line, there is a possibility of the existence of the molecular recorder in the nucleus that records many events including transcriptional events and the epigenetic process including chromatin remodeling [7-11].

In other words, all stimuli, including physical, chemical, sensory, emotional, psychological, behavioral, and nutritional and lifestyle impact our transcriptional and epigenetic events [4-11].

These transcriptional and epigenetic events are potentially recordable in the nucleus by the possible molecular recorder system either by the synthetic tools like CRISPR editing tools or by the natural molecular recorder system in the prokaryotic and eukaryotic system [8-11]. The CRISPR system is a form of adaptive immunity in the prokaryotic system and naturally this tool is used to record multiple events like DNA integration and transcriptional events [8-11]. However, the use of CRISPR tools as a molecular recorder in the eukaryotic system is debatable and needs substantial evidence. In the future, applications of synthetic CRISPR tools as a molecular recorder and the discovery of natural molecular recorder like CRISPR in the eukaryotic model will bring revolution in synthetic, basic and translational biology.

To elucidate another distinct use of CRISPR/Cas tool, an elegant article emphasizes on the contribution of liquid-liquid phase separation mechanisms involving intrinsically disordered proteins in the nucleus of the cell to bring genome organization and reorganization as a part of cellular regulation [9]. In the cell nucleus, liquid-liquid phase separation of intrinsically disordered proteins (IDPs) is implicated in the assembly of the nucleolus, as well as transcriptional clusters, and other nuclear bodies. However, it remains unclear whether and how physical forces associated with nucleation, growth, and wetting of liquid condensates can directly restructure chromatin [8-11]. In this paper, the authors delineate the role of intrinsically disordered proteins in chromatin organization to create euchromatin and heterochromatin regions using technology as CasDrop, a form of novel CRISPR-Cas9-based optogenetic technology.
This paper discusses the convergence of physical phenomena, including stiffness and mechanical energy brings order and disorder of chromatin regions as a part of nuclear regulation. In the present commentary, the author extends the existence of mechanical sensing and liquid-liquid phase separation of intrinsically disordered proteins (IDPs) in chromatin regulations as one of indirect evidence to support the potential existence of molecular recorders to record the epigenetic events in the chromatin assembly and re-assembly.

In a speculative model of chromatin assembly and re-assembly, the findings hint on an existence of a model of elastic rubber and spring model where twisting and untwisting involve mechanical and physical phenomena and these processes can be recorded by possible molecular recorders in the nucleus [4-11].

In short, both models of mechanical sensing and liquid-liquid phase separation of intrinsically disordered proteins (IDPs) in chromatin regulations and molecular recorders in the perspectives of chromatin regulations appear to indirectly support each other [8-11]. In a similar direction, we have also hinted a speculative model of the existence of epigenomic hard drive in the nucleus of cells that may employ molecular recorders besides the existing views on the presence of the epigenetic molecular reader, eraser and write to achieve the recording of chromatin remodeling and transcriptional events.

FUTURE IMPACT

The existence of molecular landscape to record chromatin remodeling and transcriptional events in prokaryote and eukaryote appears to be a key phenomenon. However, clear evidence of these molecular mechanisms is lacking. Currently, some convincing findings support the functioning of such events. Besides this, possibilities of the use of designer molecular recorders in the form of a CRISPR/Cas system like Cas-Drop and Cas-Spacer technologies may help to record chromatin remodeling and transcriptional events in higher organisms. The potential use of these molecular recorder tools lies in the decoding of altered chromatin remodeling and transcriptional events in case of several pathophysologies, including cancer, neurodegenerative disorders, diabetes, etc. that may eventually help in better therapeutics and diagnosis success.

REFERENCES


Nilesh Kumar Sharma
(Associate Professor)
Cancer and Translational Research Lab
Department of Biotechnology
Dr. D. Y. Patil Biotechnology & Bioinformatics Institute, Pune
Dr. D. Y Patil Vidyapeeth Pune, MH, 411033
Tel: +91 7219269540
E-mail: nilesh.sharma@dpu.edu.in