Cite this as: Xue-hun GUO, Dong YANG, Xiang-yuan ZANG, 2019. Epigenetics recording varied environment and complex cell events represents the origin of cellular aging. *Journal of Zhejiang University-Science B (Biomedicine & Biotechnology)*, 20(7):550-562. https://doi.org/10.1631/jzus.B1800507

Epigenetics recording varied environment and complex cell events represents the origin of cellular aging

Key words: Epigenetics, Environment, Cell event, Cellular aging, Epigenome entropy, DNA methylation

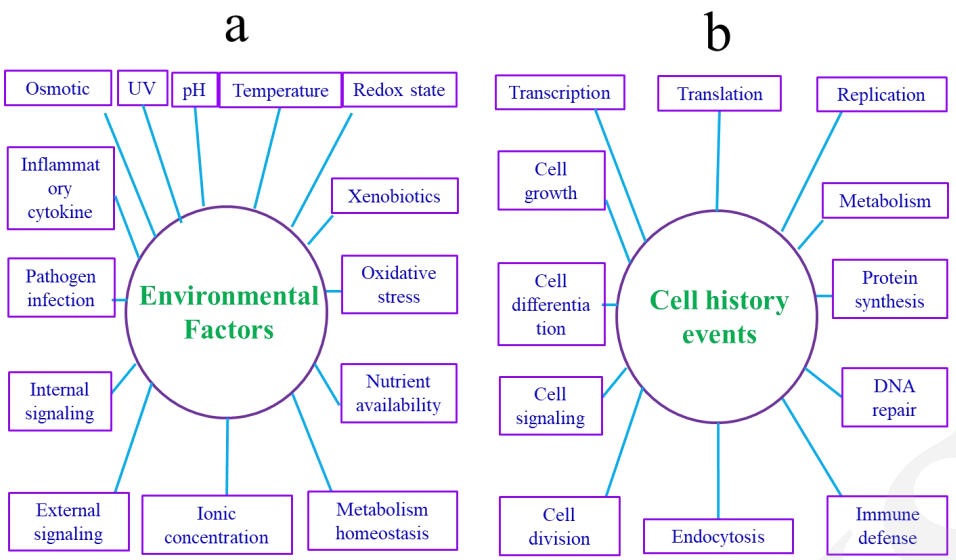

Fig. 1 (a) Cells live in an unpredictable environment comprising many diversified environmental factors and (b) undergo a wide variety of cellular historical events.

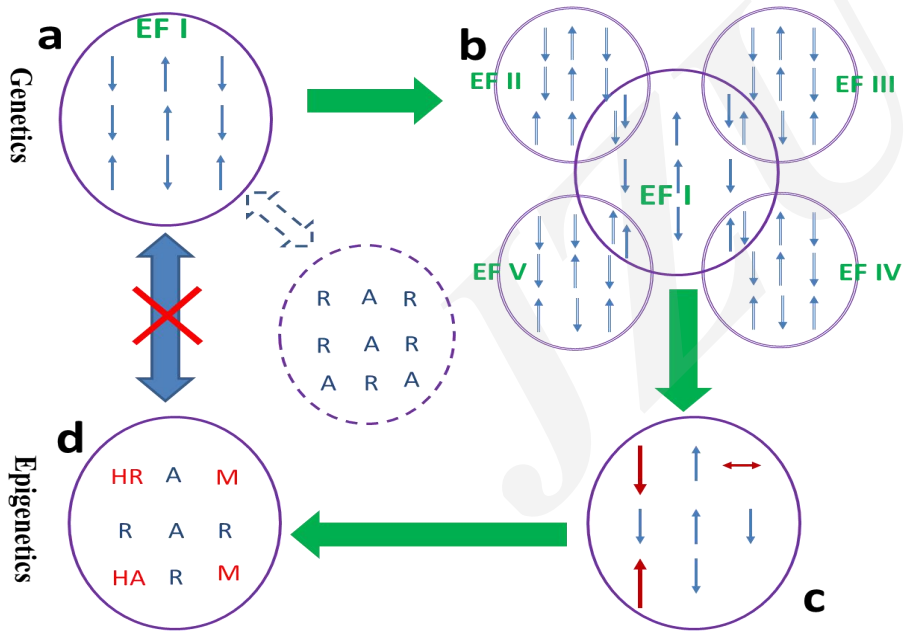

Fig. 2 Varied environment factors produce irreconcilable conflict between the ideal genetic regulation and the suboptimal epigenetic state. (a) a specific collection of gene variations, up(↑) or down(↓) regulated, are involved to answer a specific environmental factor (EF I) ; **(b)** But actually, cells are exposed to and inevitably have managed to answer some other different environmental factors (i.e., EF II, EF III, EF IV, EF V, …); **(c)** both the synergistic (↑ or ↓, vertical arrows) and antagonistic (↔**,** horizontal arrows) effect can be generated in the assembly pattern of gene expression in answer to all of these varied environmental factors; **(d)** Imprinted by these varied environmental factors, a spectrum of epigenetic states could be generated in the related regions of chromatin ('A', activated epigenetic state; 'HA', highly activated epigenetic state; 'R', repressive epigenetic state; 'HR', highly repressive epigenetic state; 'M', medium epigenetic state); Consequently, the irreconcilable conflict between the ideal genetic regulation (a) and the suboptimal epigenetic state (d) would be conveyed in answering each environmental factor; **(e)** a perfect match between the ideal genetic regulations and actual epigenetic states in answering each specific environmental factor (here refers to EF I) actually does not exist.

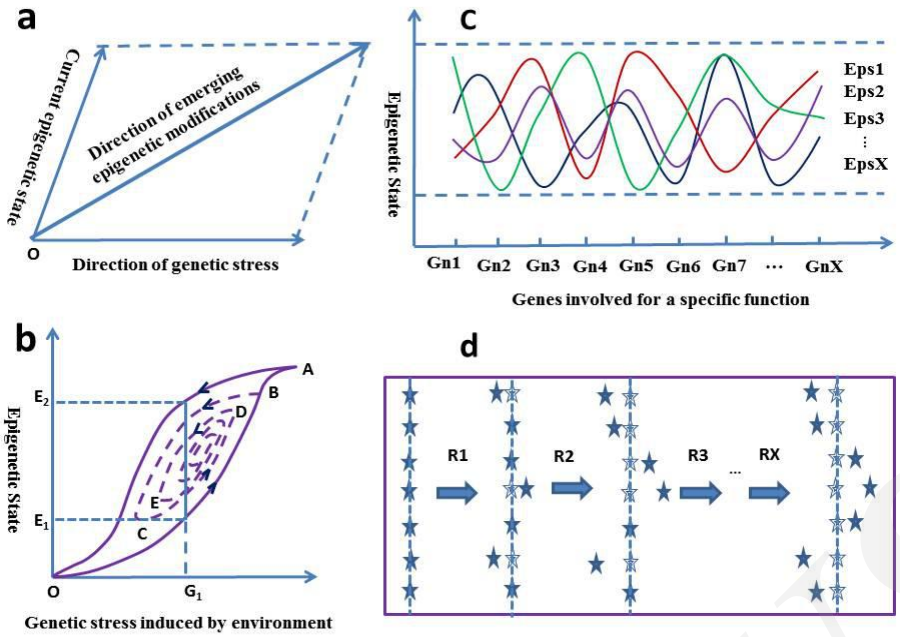

Fig. 3. Irreversibility and hysteresis of epigenetic modifications in response to new environment and emerging events would inevitably lead to a dissipated spectrum of chromatin state with increasing loss of epigenome entropy. (a) cells make compromised epigenetic modifications between the epigenetic records and stresses derived from environment; (b) Epigenetic hysteresis may produce a range of epigenetic states (from E_1 to E_2) when confronted with a specific genetic stress (G_1); (c) Hysteresis thereby results in epigenetic drift, where the epigenetic states (Eps1, Eps 2, Eps3, …, EpsX) of different cells at each gene locations (Gn1, Gn2, Gn3, …GnX) vary greatly in a specific environment (Gn: gene; Eps: epigenetic state); (d) The epigenetic state at each gene location (symbol of five-point stars) is first at their beginning position. After a series of round-trip change (R1, R2, R3, …, RX) in specific cellular events or environmental parameters, dissipated patterns of epigenetic states are generated due to the different degree of hysteresis for different gene locations.

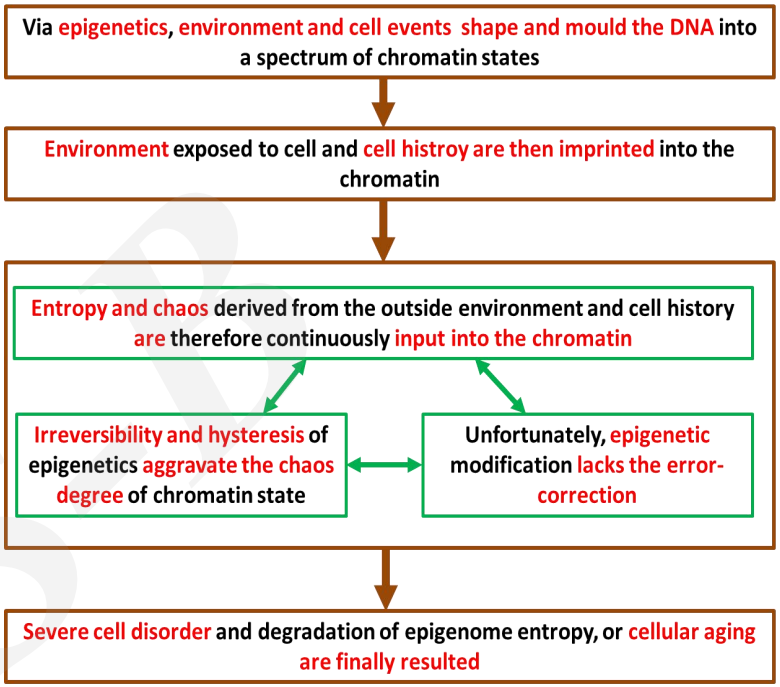

Fig. 4. Outside entropy (or chaos) derived from the varied environment and complex cell history, gradually input and imprinted into the chromatin via epigenetic modifications, would lead inevitably to cellular aging, the extent of which could be aggravated by hysteresis of epigenetics without error erasing and correction.