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Evolutionary Genetics and Genomics

Intron Retention as a Bidirectional Homeostat: Stress Fingerprints and Therapeutic Readouts

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Time: 2026. 03. 05 Thu. 15:00
Venue: Auditorium, 1st Floor
Interdisciplinary Research Building
跨領域科技研究大樓1 樓演講廳
Host: Dr. Chih-Ming Hung 洪志銘副研究員

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Abstract

Several years ago, we discovered that in an aging mouse model, specific introns from dozens of genes reproducibly accumulate compared with wild-type controls. Strikingly, this "IR load" (intron retention, IR) is not irreversible: it reverts toward a healthy pattern when metabolic status is improved by Japanese herbal medicine. Subsequent work revealed that this is not an aging-specific curiosity but a general response to a broad spectrum of stresses. Importantly, stress elicits a bidirectional IR program—some introns accumulate (IncIR), while others are actively reduced (DecIR). The genes exhibiting these intron changes (IRGs) are stressor-specific, meaning that IRG profiles can serve as molecular fingerprints to identify the type of stressor. Clinical studies further indicate that IR dynamics in patients' blood can quantify recovery trajectories and even report the efficacy of medications themselves. Together, these observations suggest a unifying model in which stress-induced deviations in protein concentrations are counterbalanced by IR: IncIR dampens protein output, whereas DecIR restores it, thereby functioning as a tunable "IR-Homeostat" that stabilizes the proteome under fluctuating demands. In this presentation, I will introduce the experimental evidence leading to this hypothesis, highlight its testable predictions, and discuss how IR-based readouts could enable stress typing and response-guided medicine. Finally, I will discuss mechanistic routes by which IR may couple RNA processing to proteostasis and how this framework can be validated experimentally.