In recognition of the discovery of two riboswitch classes that selectively respond to PRPP\(^1\) and ppGpp\(^2\), and in recognition of the hypothesis that certain common RNA-derived signaling molecules might be relics of the chemical ‘language’ of RNA World organisms\(^3\), the status of Breaker Laboratory “Molecule of the Year” is conferred upon these findings.

Many known riboswitch classes are triggered by RNA-derived metabolites, suggesting that some riboswitches might be of ancient origin. This hypothesis is further supported by the discovery\(^1\) of riboswitches for PRPP (Fig. 1A), which is the first committed step in the biosynthesis of RNA nucleotides. PRPP riboswitches therefore sense the key first step for the production of their own building blocks. Similarly, the discovery\(^2\) of riboswitches for ppGpp (Fig. 1B) reveal another link between RNA-based signaling molecules and RNA-based sensors.

Ancient RNA World organisms would have likely used derivatives of RNA building blocks to serve as signaling molecules\(^3\). Such compounds still exist in modern cells in the form of common alarmones such as ppGpp and ZTP, and second messengers such as c-di-GMP and c-di-AMP. It seems probable that the common RNA-based signaling molecules in extant biological systems first emerged as a form of RNA World ‘language’.

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