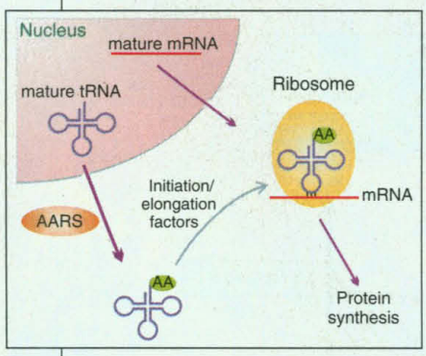
Frontiers in Cell Biology: Quality Control

Cells are the basic building blocks of living organisms, and the cell can be pictured as a very complicated factory of life. In order to maintain an effective internal regime and to prevent inappropriate attack by external factors, the cell needs quality control mechanisms to identify, correct, and prevent mistakes in its ongoing processes. The consequences of faulty quality control range from the cell death of neurodegeneration to the uncontrolled cell growth that is cancer.

In the special section in this issue, four Reviews describe four key processes in the cell and examine what is known about their quality control mechanisms. Ellgaard *et al.* (p. 1882) look at quality control in the secretory pathway. Cells must avoid expressing misfolded or incorrectly assembled proteins on their surface in order to prevent immune attack. The cell has developed an efficient set of quality control mechanisms at the entry step of the secretory pathway, the endoplasmic reticulum. Only correctly folded and assembled proteins are allowed to travel further for eventual release from the cell by secretion or for insertion into the cell surface.

Wickner *et al.* (p. 1888) concentrate on posttranslational quality control in the cytosol. During protein synthesis (translation), the cell uses a surveillance system to recognize aberrant proteins, which may arise from mutation, errors in translation, or the cytotoxic effects of heat or chemicals. The major components of this system are the molecular chaperones and energy-dependent proteases. Wickner *et al.* outline a model for recognition of aberrant proteins during a process of molecular triage, directing salvage and refolding of damaged proteins where possible and destruction if not. Failure of quality control may lead to protein aggregation. Pathological protein aggregates are linked to a variety of neurodegenerative diseases, including Parkinson's disease.



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Ibba and Söll (p. 1893) describe quality control as protein synthesis occurs and at the steps immediately preceding protein synthesis. During cotranslational quality control, through the processes of proofreading and editing the cell can prevent misincorporation of amino acids into the nascent polypeptide chain. Messenger RNAs are also monitored before translation to prevent synthesis of protein from an error-laden message. Additionally, during the synthesis of transfer RNAs, the cell selects the correct amino acid for the correct codon. Together these mechanisms maintain a very low error rate in amino acid incorporation—under normal growth conditions, only about 1 in 10,000 codons is misread.

Lindahl and Wood (p. 1897) discuss how the genetic material itself—the chromosomal DNA in the cell's nucleus—is subject to quality control in order to ensure the retention of a faithful copy of the cellular genome. Damage can occur from exposure to sunlight or to harmful chemicals. Cells possess a variety of DNA repair mechanisms, whose relative importance in preventing pathological mutations is discussed. Failure of quality control can lead to mutation and cancer. For example, DNA repair enzyme mutations are linked to xeroderma pigmentosum and ataxia telangiectasia.

Quality control is vital for maintaining a fully functional cell. The cell expends much energy in ensuring faithful completion of its synthetic processes and in disposing of inappropriate products. Failures in quality control are involved in multiple pathological processes and are likely to be a fundamental factor in aging. As with most things with multiple potential pitfalls, the miracle is that cells function at all.

–STELLA M. HURTLEY

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