Research Discoveries / Significant Contributions to Science

Molecular biology contributions

- Evidence for potential informational instability in biological processes – protein synthesis errors in *E. coli* can feedback, become progressive and unstable (Nature, 1975) [paper was reprinted in the *Benchmark Papers in Genetics* series].

- Demonstrated an inverse relationship between ribosome speed and the fidelity of protein synthesis discovered using *E. coli* ribosomal mutants: defined kinetic parameters of accuracy in the translation of the genetic code (Nature, 1976).

- A bacterial protein severely bends DNA at specific binding sites – the most severe such effect ever observed: The IHF protein bends DNA approximately 120o (bending discovered at both ends of the transposable insertion sequence IS1) (1984).

- The transposition rate of insertion sequence IS1 is regulated by translational (ribosome) frameshifting on the mRNA transcript – fused transposase protein competes with unfused repressor. This discovery defined a novel regulatory mechanism, for regulating the movement activity of bacterial transposable genetic elements (1987).

Footprinting

- Devised the “DNA footprinting” method for defining the exact position of DNA-binding proteins on their binding sites. This is the first and still most widely used method for defining exact protein binding sites on the DNA and now can be used *in vivo* (published,1978).

Human gene discovery

- Susceptibility to early onset Alzheimer’s disease can be caused by missense mutations in a membrane protein gene (presenilin 2, or “PS2”). The mutant protein mis-processes amyloid protein as well as others. This protein is now recognized as one of two gamma-secretase enzymes involved in amyloid protein processing (Science, 1995).

- First identified human gene that affects the human rate of aging. The Werner’s Syndrome gene is a DNA helicase. Galas conceived of and led a collaborative project team that found the gene by positional cloning (1996).

- Discovered a gene in both mice and humans that, when mutated, leads to a serious lymphoproliferative disorder. The FoxP3 gene causes severe hyper-inflammatory response of the immune system. The X-linked gene inactivation is fatal in infancy in human males (called IPEX.) This protein we called *scurfin* is encoded by gene FoxP-3. It is a key transcription factor in the development and stability of regulatory T-cells (Nature Genetics,1997). The Crafoord Prize of the Swedish Royal Academy (in 2017) was awarded to young Team member Fred Ramsdell, who connected FoxP3 to Treg cells.
- New human gene regulating bone mineral density called SOST. The recessive genetic disorder, sclerosteosis, is caused by loss of gene function in a gene encoding cystine-knot protein called sclerostin. Identified a new pathway for regulation of bone mineral metabolism (involving the Wnt pathway). An Ab to this protein is an FDA-approved therapeutic for osteoporosis (FDA approval 2017).

NAAT

- Discovered a new class of isothermal nucleic acid amplification reactions and invented several schemes for developing diagnostic tools using them. The biotech company, Ionian Technologies Inc., was founded based on this discovery/invention (in 2002). Several diagnostics based on this technology are now FDA-approved (flu A, flu B, RSA, Covid19 coronavirus).

Bioinformatics methods

- Galas developed a class of information theory-based statistical measures that provides computational tools for determining dependencies among variables in complex biological data. This has developed into powerful methods for analyzing genetic data for human and model organism genetic data (several papers, J Comp Biol, etc.).

Quantitative genetics

- The information theory measures mentioned above can be used to reformulate quantitative genetics, which has now been done (published in J Comp Biol, 2020).