Propositions Accompanying this Thesis

Complexity of Genomic Actions Controlled by Thyroid Hormone Receptors

1. Studying novel mutations in thyroid hormone receptors that occur in patients provides important molecular insights into the role of particular amino acid residues/domains in receptor functions. *(This thesis)*
2. Met256 in thyroid hormone receptor α1 and the equivalent Met310 in thyroid hormone receptor β1 dictate preference for T3 over T4 of the thyroid hormone receptors. *(This thesis)*
3. The severity of the clinical phenotype of resistance to thyroid hormone α patients carrying the missense mutations is related to the reduced T3 binding affinity of the mutant receptors. *(This thesis)*
4. In the group of thyroid hormone receptor α1 truncating mutants that exhibit negligible T3 binding, the severity of the patients' phenotype is related to the capability of the mutant receptor to alter baseline gene expression. *(This thesis)*
5. A subset of coregulatory proteins interacts with thyroid hormone receptors in cell-type and isoform-specific manners. *(This thesis)*
6. Understanding mechanisms of thyroid hormone receptor mediated gene transcription would allow the development of customized approaches to manipulate thyroid hormone signaling, with enormous therapeutic implications. *(adapted from Bianco AC et al., Endocr Rev 2019;40(4):1000-1047.)*
7. Integrating multi-dimensional OMICs data will generate novel insights into system-level gene regulations and serves as a foundation for further hypothesis-driven research. *(Qin J et al., Quant Biol 2016;4:283-301.)*
8. Given the rapid pace of changes in the field of the clinical genome and exome sequencing, all medical providers should keep a weather eye open for changes in this transformative field. *(adapted from Adams DR et al., N Engl J Med 2018;379:1353-1362.)*
9. The optimal conduct of science and its application to problems in medicine require a critical mass of investigators who regularly collaborate, critique each other's work, and serve as each other's sounding boards for new ideas and techniques. *(Schor NF. Neurology 2013;80(22):2070-2075.)*
10. The great discovery that launched the scientific revolution was the discovery that humans do not know the answers to their most important questions. *(Yuval Noah Harari)*
11. No matter what your ability is, effort is what ignites that ability and turns it into accomplishment. *(Carol S. Dweck)*

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