After decades of research unraveling complex metabolic control networks, medicines capable of a safe reversal of type 2 diabetes are still not available. Historically, complex diseases have repeatedly proven to be defiant to the best mono-therapeutic approaches. Several examples of combination therapies have largely overcome such challenges, notably for the treatment of severe hypertension and tuberculosis. Obesity and its consequences, such as type 2 diabetes, have proven to be equally resistant to therapeutic approaches based on single medicines. Appropriate management of type 2 diabetes often requires adjunctive medications, and the recent registration of a few compound mixtures has set the precedent for combinatorial treatment of obesity. On the other hand, double or triple therapeutic combinations are more difficult to advance to regulatory approval. Following an improved understanding of the molecular basis for metabolic benefits following bariatric surgery interventions, several classes of novel unimolecular or independent combination therapeutics were discovered. These new classes of drug candidates are based on gastrointestinal hormones, offer efficacy superior to currently prescribed options and seem to have potential to fully reverse human obesity and type 2 diabetes. Moreover, gut peptide-based cell-specific targeted delivery of small molecules offers additional potential for novel metabolic precision medicines and reduced systemic side effects. In this presentation the discovery, pre-clinical validation and first clinical tests of peptide hormone poly-agonist drug candidates as well as of combinatorial single molecule therapeutic candidates will be summarized, including previously unpublished observations.

Conflict of Interest: Scientific Advisory Board: Novo Nordisk, ERX Biotech; Consultant Bionorica SE

Bibliography
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