Developing Novel Non-Hormonal Female Contraceptives; Targeting the FADS1-COX2-PGE2 Pathway

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Many oral birth control pills for blocking ovulation contain primarily progestin, a synthetic sex steroid hormone of progesterone. However, current oral contraceptives containing hormones can cause serious side effects such as depression, hormone-related cancers, and stroke. Unfortunately, there is a lack of effective screening platforms which has impeded the development of novel non-hormonal female contraceptives. With there currently being no non-hormonal birth control pill available on the market, we wanted to elucidate the FADS1-COX2-PGE2 pathway, a crucial signaling underpinning ovulation, and identify key knowledge gaps to develop a model to optimize our leads for better efficacy. A complex 3-tiered drug screening system was utilized to locate optimal druggable candidates. Literature reviews were conducted utilizing PubMed as the primary database and [20] primary research articles were selected to locate key knowledge gaps in this target pathway. Understanding these pathways will allow us to better evaluate the non-hormonal contraceptive promises of our compounds. With our compounds being shown to inhibit the FADS1-COX2-PGE2 pathway, we aim to establish a model to identify potential contraceptive analogs. Quantitative structure activity (QSAR) analysis in drug discovery describes how changes in a molecule's chemical structure affect its biological activity, which facilitates the design of effective and safer compounds for more advanced drug development activities. QSAR models will be developed to locate core chemical structures of analogs and ensure the safety of these lead compounds. These findings will aid in establishing a platform for identifying and validating contraceptive candidates, furthering research regarding women's reproductive health. Supported by the Gates Foundation INV-003385, NIH/NIEHS R01ES032144, and NIH R25ES020721, the RISE Program, the Ernest Mario School of Pharmacy, and the Society of Toxicology.