Session OR17 - Reproductive Biology I

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# O-052 - Drug-Target Model for Discovering and Personalizing Endometriosis Therapies.

📅 March 14, 2019, 5:45 PM - 6:00 PM | 📍 Room 241

## Categories

+11.0 - Basic Reproductive Biology: General

## Keywords

Systems pharmacology,protein-protein interaction network,endometriosis drugs

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## Abstract

**Introduction:** Gene-disease associations produced by molecular and genetic studies of complex diseases as endometriosis, provide great opportunities for understanding drug activity at a system-level. We aim to analyze the systems pharmacology relationship between endometriosis-related drugs and targets to discover new therapies for Precision Medicine in endometriosis.

**Methods:** Endometriosis treatments were consulted from ASRM and ESHRE guidelines to select established endometriosis-related drugs. Endometrial tissue-specific diseases genes were prioritized from type III-IV endometriosis patients from GEO datasets (GSE6364, GSE7305 and GSE11691) using an integrative differential expression analysis between ectopic vs eutopic endometrial samples (FDR<0.05). DrugBank, which is a reference database providing detailed information about pharmacokinetics and pharmacodynamics drug action, was consulted to obtain information about targets-related to approved drugs in humans. We used Cytoscape software and The Human Interactome to build a protein-protein interaction network based on endometriosis-related targets and drugs and their potential interacting drugs and targets. Network topology, tissue and cellular location were parameters used to prioritize new targets and drugs from a systems pharmacology point of view.

**Results:** Our model was significantly enriched for endometriosis related genes (p-value < 2.2e-16), that reinforced the network emerging properties to predict drug action and potential targets. New drug groups based on different chemical structure that target hormone receptors were found such as Zinc therapy, whose deficiency has been reported in women with endometriosis. Additionally, new targets as SRC, that has a direct physical interaction in our network with PGR and ESR1 steroid receptors, and other targets non-related to steroids as AQP1, were discovered as a potential alternative pharmacologic therapy in endometriosis. Furthermore, some of the interacting drugs highlighted by our model are currently therapies under experimental research for endometriosis as Verapamil or Cisplatin, and we also discovered new ones non-proposed before as Ponatinib.

**Conclusion:** Although new studies are needed to test the new potential therapies for endometriosis, our model has provided a comprehensive information related to approved drugs in humans for existing and new proposed therapies in endometriosis. By other hand, our model also provides molecular detailed information about signaling pathways related to the mode of action of drugs for predicting side effects and for personalizing medicine in endometriosis therapies.