

## **TIMESOME: The Human Gender Clock-genes Interactome of Biological Time-keeping. Toward mapping and timing gender chrono-pharmacogenomic individualized medicine and therapy**

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Detection of a gender genomic ID-clock information has been a longstanding unfulfilled dream in medicine. - As we coined it Timesome, it represents the internal timing machine that sustains interactome rhythms around 24 hours in the absence of external cues in man and women. . It consists of an array of genes and the protein products they encode, which regulate various physiological processes throughout the body during the daily dark/light cycle of rest/activity. The human timesome is operated by an evolutionary molecular framework clock oscillator composed of transcription/post-translation-based auto-regulatory feedback loops of the circadian genes in the central pacemaker (suprachiasmatic nucleus of the brain), as well as in most peripheral tissues (skin, liver, gastro-intestinal tract, hematopoietic system and bone marrow, retina, lung, skin, kidney and bone cells). This regulates neuro-endocrine functions in which clock gene products negatively regulate their own expression. - Deciphering Gender Pharmaco-genomic Clocks by Clinical Functional Genomics and Proteomics. We took a system-biological approach based on genomic, molecular and cell biological techniques applied to human circadian rhythms. We created a “gender ID molecular timetable” composed of genomic guardian “time-indicating genes”, whose gender gene expression levels can represent the internal genomic ID-Clock. This biotechnology approach can translate functional genomics into gender time-mapped pharmacogenomic personalized medicine, new therapeutic targets and drug discovery. Gender maps of time-keeping patterns may serve for timing, screening, diagnosis and an improved quality of life and to reveal the understanding of mechanisms underlying time-disruption in the etiology of various diseases (cancer, cardiovascular, neuro-psychiatric, gynecobstetrics, pediatrics, aging and chronic illnesses) in men and women along their lifespan.