2.	Μη τεχνική περίληψη του έργου/ Non-technical summary of the project Menopause is a universal and irreversible part of the overall aging process in a woman. However, menopause is not restricted to just the cessation of menses but to a more complex series of events that induce changes in most of the physiological systems in the body, including the neurological system. Healthy aging, encompassing body and mind, should be the goal of any woman after the age of 50+. And in order to maintain a healthy aging brain, there are still many unknown facts relating the effects of steroid female hormones in the brain. **General objectives**: To characterize how menopause impacts the main inhibitory neurochemistry system in the brain (GABAergic system), and investigate the effects of drugs used to alleviate menopause symptoms on the cognitive, cellular and molecular characteristics of the hippocampus, the brain region responsible for memory, and the retina as a model for the nervous system. Neurogenesis in the adult hippocampus is associated with formation of new memories and learning, and the inhibitory neurotransmitter GABA regulates neurogenesis, and is essential for the integration of these newly generated neurons within the hippocampal circuitry. Estrogens influence cognitive function, exert neuroprotective and neurogenic effects, and in the hippocampus, enhance GABA activity. Changes observed in brain function and the increased vulnerability observed on aging women to brain injury and neurodegenerative diseases could result not only from declining levels of estrogens but also from changes in the GABAergic system. **Methodology**: Ovariectomized young female mice receiving estrogens, phytoestrogens, GABA agonists, or placebo for 2 months will have the central nervous system (retina and hippocampus) examined for cellular and molecular changes **Main implementation activities** originating from the proposal will be the establishment of an animal model for menopause and the comparison of the different treatments on cognitive, cell and molecular aspects of the brain. We will also build the cellular and molecular basis for establishing the potential beneficial effect of GABA for alleviating cognitive changes in menopause. **Anticipated results**: We expect to see a decrease in the expression of the GABAergic system markers in the mouse model of menopause, and a substantial recovery following the different treatments. Senescent monkeys have decreased number of GABAergic neurons and application of GABA or agonists improve their visual function. Because of the neuroprotective and neurogenic effect of the hormones, we also expect to find increased neuronal proliferation, number of GABAergic neurons, GAD enzyme protein and mRNA levels. **Benefit**: Menopause Hormone Therapy is still a very controversial issue, because of the potential adverse effects on the health of the individual. Despite this, animal studies have shown that the beneficial effects are unsurpassed. If drugs used in MHT show an effect in a specific neuronal population (GABAergic), this population itself could become a potential therapeutic target (hormonal or not) for improvement of cognitive functions in aging. GABA agonists have already been used as an alternative non-hormonal therapy to treat hot flashes. Our research is innovative and points for a potentially new therapy, not only for the vasomotor symptoms, but also to rescue and perhaps reverse the decreased cognitive function, circumventing the adverse effects of the drugs used in MHT. The animal study will help us identifying the most effective form of intervention, which

	might be employed in a pilot human study. Finally, the implications of the present research proposal will have an **impact in the quality of life** of the female adult and elderly population in Cyprus, improving the standard of living of the elderly female citizens, improving their cognitive capabilities and in the long run, promoting their mental health by having an effect in the prevention of neurodegenerative diseases that affect elderly population, such as Alzheimer's disease.