



**Name:** Luca Clemente

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**Major Professor:** Paul Bertics

**Degree Objective:** Ph.D. Endocrinology and Reproductive Physiology

**Background:** BS Biochemistry, Colorado State University, CO.

**Current Research Project:**

An oncogenic mutation of the epidermal growth factor receptor (EGFR) discovered in glioblastoma results in a high fidelity duplication of the kinase domain. Whereas wild-type EGFR is expressed at the plasma membrane and is dependent on ligand binding and dimerization for activation and internalization, this tandem kinase duplication mutant (TKD-EGFR) is primarily localized intracellularly in monomeric form and exhibits constitutive tyrosine kinase activity. The focus of my research is to determine the mechanisms responsible for the novel properties of TKD-EGFR. Recent x-ray crystallographic evidence strongly suggests that wild-type EGFR monomers dimerize asymmetrically, with one partner acting as an “activator” while the other serves as a “receiver.” The presence of two kinase domains occurring in the same receptor monomer may offer a novel mechanism for the constitutive phosphorylation of the TKD mutant. To test the possibility that TKD-EGFR forms an in cis asymmetric dimer, I am performing site-directed mutagenesis to create altered forms of TKD-EGFR in which point mutations of key residues disrupt the formation of the dimer interface. If the constitutive activity of TKD-EGFR is dependent on in cis asymmetric dimerization, strong inhibition of kinase activity following such point mutations would provide the first evidence. I will also map the trafficking of TKD-EGFR using a pulse-chase protocol and/or other real-time fluorescent imaging techniques.

**Honors:**

**Grants Received:**

**Publications:**

Wilson AC, Clemente L, Liu T, Bowen RL, Meethal SV, Atwood CS. Reproductive hormones regulate the selective permeability of the blood-brain barrier. *Biochim Biophys Acta*. 2008 Jun;1782(6):401-7.

**National Presentations:**

**Other Presentations:**

Luca Clemente, Brian Ozer, Greg Weipz and Paul Bertics. A Glioblastoma Multiform Associated Epidermal Growth Factor Receptor Mutant Possessing a Tandem Duplication of the Kinase Domain Exhibits Increased Basal Autophosphorylation Altered Localization. ERP Annual Symposium 2010.

**ERP Service:**