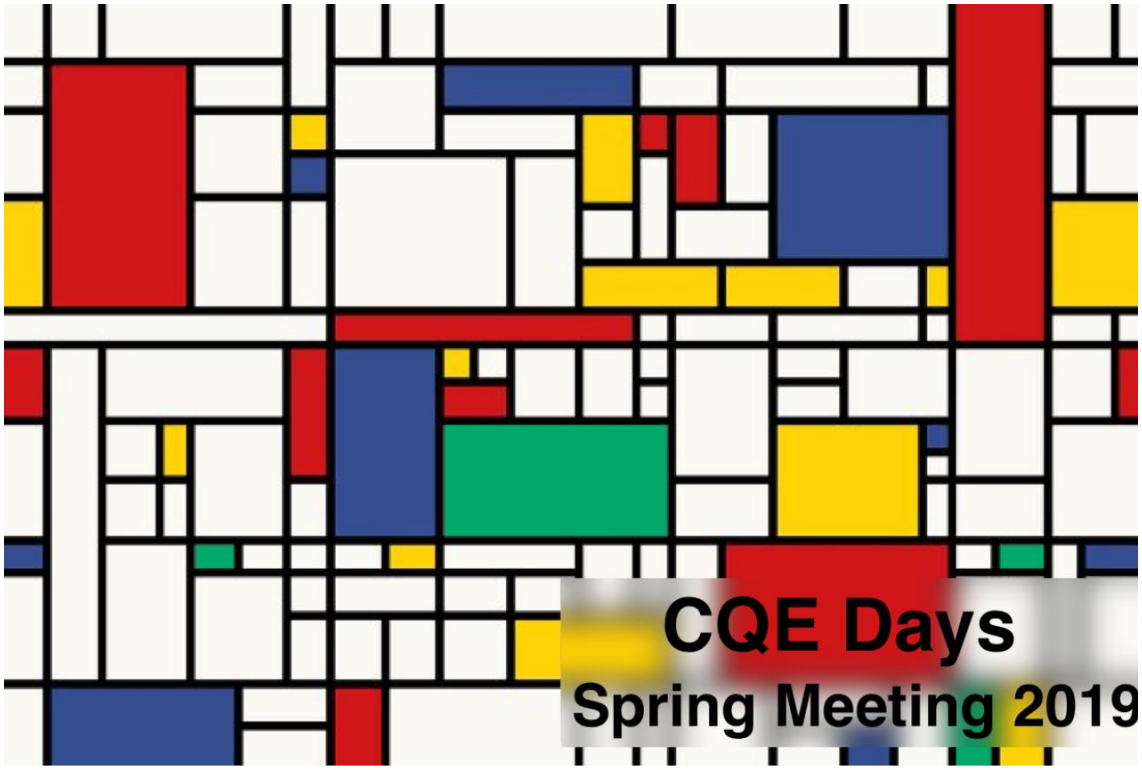

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ABSTRACTS BOOK

KEYNOTE, ORAL & POSTER

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TBCCD1: a new player in the development of ciliopathies?

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Abstract:

Cilia are hair-like appendages, consisting of a microtubule (MT)-based ciliary axoneme, which fulfill critical motility and sensory functions required for normal embryonic development and also for homeostasis of adult tissues. At their base, cilia have a centriole/basal body, which can be derived from the centrosome, and that nucleates the ciliary axoneme. Centrosomes consist of a pair of centrioles surrounded by the pericentriolar matrix that nucleate/organize the cytoskeleton and are implicated in cell migration, adhesion and polarity, while during mitosis they assist spindle pole formation (1). Centriolar satellites are cytoplasmic granules that are located and move around the centrosome. These particles are involved in centrosome assembly and primary cilium formation by delivering cytoplasmatic centriolar/centrosomal components to the centrosome (2). Mutations in genes encoding centrosome and/or centriolar satellite components and regulators lead to various human disorders such as ciliopathies. Ciliopathies are typified by often overlapping clinical manifestations e.g. infertility, obesity, brain and skeletal developmental problems, blindness and kidney cysts.
Published work from our group identified a new centrosomal TBCC domain-containing human protein (TBCCD1) that is involved in centrosome correct positioning and primary cilia assembly (3). Our recent data showed that in mammalian cells TBCCD1 is observed at pericentriolar satellites, in basal bodies of primary and motile cilia, and at the primary cilia ciliopathy hot domain, the transition zone. Super resolution microscopy showed that TBCCD1 is localized at the distal region of the centrosome and its depletion dramatically affects the centrosome subdistal protein CEP170, a component of primary and motile cilia basal feet. We used a BioID approach to define the TBCCD1 interactome and included among the identified proteins were several well-known proteins encoded by ciliopathy genes, e.g. OFD1, a centrosomal and centriolar satellites protein. The *ofd1* gene is mutated in the Oral-facial-digital syndrome, an X-linked dominant ciliopathy characterized by oral anomalies, facial dysmorphism, polydactyly and defects of the CNS like microcephaly. We showed that TBCCD1 knockdown and overexpression in hTERT-RPE1 cells affects OFD1 distribution. To clarify the role of human TBCCD1 in cilia biogenesis we used the ciliate *Paramecium* as a biological model. Noteworthy, in *Paramecium* TBCCD1 knockdown causes abnormal basal body associated rootlets organization, anomalous basal body positioning/anchoring defects. Our data using human cells and the ciliate *Paramecium* support a role for TBCCD1 in centrosome structure maintenance and in basal body anchoring at the cell membrane. These results set the tone to take TBCCD1 into account as a novel protein with a role in human ciliopathies.

Keywords: TBCCD1, Centrosomal satellites, Basal body, Microtubules
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