

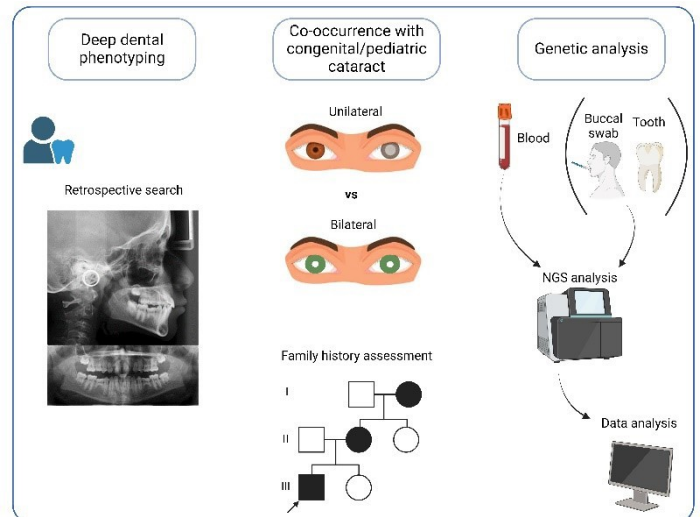
Project's title: "Exploring associations between dental anomalies and congenital cataract"

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Laboratory: Laboratory of Mendelian and Complex Diseases; Unit of General Biology and Medical Genetics

Background:

Congenital cataract (CC) is the major cause of treatable childhood blindness and impaired vision worldwide with a global prevalence of 4.24/10,000. In most cases, CC manifests isolatedly, whereas more rarely with other ocular or systemic features. Some rare syndromic forms of CC, such as X-linked conditions Nance-Horan syndrome (NHS – MIM #302350) and oculo-facio-cardio-dental syndrome (OFCD – MIM #300166), often include dental anomalies, such as Hutchinson's/ "screwdriver-shaped" incisors, and numerary defects (ranging from dental agenesis to oligodontia). Therefore, dental professionals could become more aware of their role as first-line specialists involved in the diagnosis of such very rare syndromes since dental findings are highly pathognomonic.



Scientific hypothesis and methods:

In a previous genetic study, we observed that even individuals carrying pathogenic variants in genes primarily associated with non-syndromic forms of CC exhibited dental anomalies (mainly numerary). Moreover, in some cases dental anomalies preceded the development of cataract, often unilateral. This evidence led us to hypothesize a deeper connection between cataractogenesis and odontogenesis, not limited exclusively to syndromic forms of CC.

In this project, retrospective search will be conducted on panoramic radiographs collected over time at the Unit of Orthodontics and Pediatric Dentistry of the University of Pavia. The main dental features under investigation will consist of Hutchinson's incisors, mulberry molars, supernumerary teeth, microdontia, oligodontia, and tooth agenesis. Additionally, lateral cephalometric radiographs will be collected, and cephalometric tracing will be performed to evaluate skeletal parameters, like Angle's skeletal Class and sella turcica analysis. The differential diagnosis with other non-genetic conditions, such as congenital syphilis, will also be carefully evaluated. These data will be combined with any evidence of cataract in probands and relatives. After the collection of informed consent, enrolled participants will undergo genetic analysis by Next Generation Sequencing (NGS) on genomic DNA obtained from peripheral blood samples. Potential low-level mosaic variants will be further evaluated on additional tissues, such as buccal smears and teeth, if available.

The PhD candidate will deal with cephalometric analysis, as well as the most recent DNA sequencing approaches and related bioinformatic analyses.

One of the ultimate goals of this study is to strengthen the potential interactions between orthodontics and genetics, which have so far been little explored, especially in the field of rare genetic diseases.