

Oligodontia-Colorectal Cancer via AXIN2 Gene Sequencing – Test #719

Brief Description of Clinical Features: Oligodontia is a congenital condition where six or more permanent teeth fail to develop (Matalova et al. *J Dent Res* 87:617-623, 2008; Coster et al. *J Oral Pathol Med* 38:1-17, 2009). Often, oligodontia is included as a symptom of a syndromic genetic disorder, as in the case of Charcot-Marie-Tooth or Cleft lip/palate syndromes. However, oligodontia can also occur as an isolated condition (i.e. non-syndromic), without any other readily apparent symptoms. Several genes are known to be involved in oligodontia and tooth agenesis, including *MSX1*, *PAX9* and *AXIN2* (Nieminen et al. *Eur J Hum Genet* 9:743-746, 2001; Nieminen et al. *J Dent Res* 82:1013-1017, 2003; Mostowska et al. *J Hum Genet* 51:262-266, 2006). Importantly, mutations in *AXIN2* were also found to segregate with colorectal neoplasia (Lammi et al. *Am J Hum Genet* 74:1043-1050, 2004). In patients with *AXIN2* mutations, oligodontia presented at an early age when their permanent teeth failed to develop, whereas colorectal neoplasia developed much later, usually between the ages of 30 and 60. Accordingly, screening patients with non-syndromic oligodontia for mutations in the *AXIN2* gene can be an effective way to identify individuals with a risk of developing colorectal cancer later in life.

Genetics: Oligodontia-Colorectal Cancer (OMIM 608615) syndrome is inherited in an autosomal dominant fashion. Lammi et al. (2004) described a large, four-generation Finnish family in which nine family members presented with oligodontia. All nine were found to have a heterozygous nonsense mutation (p.Arg656Stop) in the *AXIN2* gene, while none of the family members with normal dentation had the mutation. Importantly, six (67%) of the individuals with oligodontia also developed colorectal neoplasia by the age of 62. In addition to this family, the authors also screened *AXIN2* in other patients with oligodontia and identified a heterozygous frameshift mutation (p.Asn666GlnfsX40) in a 13 year old boy. Interestingly, the healthy parents of this boy were not found to have the mutation, indicating it was *de novo*. In addition to these germline mutations, several somatic frameshift mutations in *AXIN2* have been identified in colorectal tumors, further providing support for the role of *AXIN2* in the development of cancer (Liu et al. *Nat Genet* 26:146-147, 2000).

Description of This Particular Test: This test involves bidirectional DNA sequencing of all 10 exons (2-11) of the *AXIN2* gene, plus ~50 bp of flanking non-coding DNA on either side of each exon. As indicated, we will also sequence a single exon (Test #100, \$190) in family members of patients with a known mutation, or to confirm research results.

Reference Sequences: Genomic: NC_000017.10 mRNA: NM_004655.3 Protein: NP_004646.3 CCDS 11662.1

Indications for Test: Candidates for this test are patients with non-syndromic oligodontia. This test is specifically designed for heritable germline mutations and is not appropriate for the detection of somatic mutations in tumor tissue.

Sensitivity of Test: The clinical sensitivity of this test is currently unknown.

Turnaround Time: Maximum of 40 calendar days, although many tests are completed in 2-3 weeks.

Specimen Requirements: See bottom of page 4 of Requisition Form.

Price:	Sequencing of the AXIN2 Gene:	\$ 790
CPT Codes:		
Sample Ascertainment x1	83890 \$ 30	DNA Isolation x1 83891 \$ 40
Amplification x13	83898 \$ 220	Sequencing x13 83904 \$ 330
Separation x1	83894 \$ 50	Interpretation/Report x1 83912 \$ 120

Accreditation : CLIA ID #: 52D1027685 (expires 1/18/13) (CAP#: 7185561, AU ID: 1407125 expires 12/20/12)

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