

# Facial Infiltrating Lipomatosis Contains Somatic *PIK3CA* Mutations in Multiple Tissues

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**INTRODUCTION:** Facial infiltrating lipomatosis (FIL) is a rare congenital disorder that causes overgrowth of one side of the face, that can include premature dental eruption, hemimacroglossia, macrodontia, and mucosal neuromas.<sup>1</sup> We recently reported that affected subcutaneous adipose tissue in patients with FIL contains mutant cells with somatic gain-of-function mutations in *PIK3CA*.<sup>2</sup> The purpose of this study was to determine whether other affected tissues in FIL also contain mutant cells.

**MATERIALS AND METHODS:** We obtained FIL tissue from 2 patients during a clinically-indicated procedure. We isolated skin, subcutaneous fat, muscle, buccal fat, and mucosal neuroma tissues, and cultured CD31<sup>+</sup> endothelial cells. We then performed droplet digital PCR (ddPCR) on DNA from each tissue and the cultured endothelial cells to determine the frequencies of *PIK3CA* mutant alleles in the different tissues.

**RESULTS:** In one FIL specimen we identified a p.H1047R mutation that was present at allele frequencies of 5.5% in skin, 17.6% in subcutis, 23.2% in buccal fat, 12.5% in mucosal neuroma, and 1.2% in endothelial cells. In a second FIL specimen, we identified a p.H1047L mutation that was present at allele frequencies of 5.6% in muscle, 16.2% in subcutis, and 1.5% in endothelial cells (Figure 1).

**CONCLUSIONS:** Cells containing *PIK3CA* mutations are present in several different tissues that are affected in FIL. These data are consistent with the mutation arising in an early pluripotent cell gives rise to several different tissue types in the face, rather than the mutation arising in only one cell type and causing overgrowth of surrounding tissues via paracrine signaling.

## REFERENCES:

1. Padwa BL, Mulliken JB. Facial infiltrating lipomatosis. *Plast Reconstr Surg*. 2001 Nov;108(6):1544-1554.
2. Maclellan RA, Luks VL, Vivero MP, et al. *PIK3CA* activating mutations in facial infiltrating lipomatosis. *Plast Reconstr Surg*. 2014 Jan;133(1):12e-19e.

## FIGURE LEGEND:

**Figure 1.** (Left) Four-year-old female with facial infiltrating lipomatosis (FIL). (Right) Droplet digital (ddPCR) reaction showing *PIK3CA* mutation in muscle from patient with FIL. Left upper quadrant represents droplets with only the mutant allele. Right upper quadrant shows droplets with mutant and wild-type alleles. Left lower quadrant illustrates droplets that do not contain any alleles. Right lower quadrant has droplets with only the wild-type allele.

