



# Patient Report

**FAP (Familial Adenomatous Polyposis) & PJS**

A Report by  
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I need to write a bit of background on FAP (Familial Adenomatous Polyposis) and its relation to PJS. You can find good articles on FAP at [GeneClinics](#) and [OMIM](#).

FAP is the ultimate polyposis syndrome. People with the disorder develop hundreds to thousands of adenomas in their colons that have a 100% chance of becoming cancerous. Prevention in FAP used to be colostomy (colon replaced by out-of-body bag). Now it is colectomy (colon removal) and regular scoping. There are also chemo-prevention measures like the Cox-2 inhibitors I mentioned in my previous letter and Exisulind (Aptosyn). These chemo measures are aimed at preventing and reducing polyps. FAP is used as the model of the adenoma to carcinoma sequence. Because many people in the general population develop colon adenomas and some progress to cancer, researchers have followed the chain of genetic events that lead to cancer.

For many years PJS has been in the shadow of FAP. First off, we share the same doctors and researchers. The course of our syndrome is often compared to FAP. When we didn't exhibit the same malignant potential for our polyps, PJS got shuffled to the back of the agenda. Also, there are far fewer PJS folks in the registries (thirty years after its founding the Johns Hopkins registry has 34 PJS families and 316 FAP families). The numbers are similar for other registries like St. Mark's in London. Marita mentioned the 10 families in Finland. It's easy to see the researchers' problems. As Dr. Sadana said, our group has the largest number of PJS folks assembled anywhere.

The PJS to cancer pathway doesn't seem to be the same as FAP. First off, our polyps are hamartomas<sup>1</sup>. FAP polyps are adenomas<sup>2</sup>. FAP folks have a 100% risk of colon cancer, but PJS folks have lower rates of cancer in a variety of organs. There have been articles written on the hamartoma-adenoma-carcinoma sequence, but there have been no large studies done. Nor is there consensus among the researchers about this sequence. The molecular biologists who are looking at apoptosis or cell death and VEGf or angiogenesis may offer some ideas for why we get cancer.

It seems reasonable to me to try Cox-2 inhibitors on PJS folks. These drugs have a lower risk of causing GI bleeding than NSAIDs do. Though there is still some risk as recent reports on people with ulcers show. And they are being tried on every other cancer. It's going to be a little difficult to prove that they prevent cancer in PJS folks since experts' estimates of cancer risk in PJS vary from 2% to 93%. If you don't get cancer while taking Cox-2 inhibitors, does that prove you're in the 98% to 7% of people who wouldn't have gotten it? It's going to be easier to map the polyps before and after, as reported in the medscape article I wrote about last letter. It's going to be difficult for the researchers to gather enough PJS folks to join their studies to get the numbers to prove that it does or doesn't work.

There's a little more about FAP that I'd like to share. The FAP gene is on chromosome 5q and the PJS gene is on chromosome 19p13.3. A second FAP gene named APC2 was recently mapped to 19p13.3.<sup>3</sup> Chris Amos kindly shared a copy of this report with me and gave some interesting comments. The gene is near but not at the PJS locus. Both genes

are near the markers for adenoma malignum of the uterine cervix (a rare form of cervical cancer associated with PJS). And about 50% of ovarian cancers contain LOH on 19p13.3. I find this interesting for many reasons. It is possible that some PJS folks have mutations that affect all of these loci, while others have mutations that are just confined to the PJS locus and give just PJS. We could live in a really bad genetic neighborhood that affects our risk for various cancers. Since most FAP folks have a mutation of 5q, researchers may reanalyze those who don't for mutation at 19p13.3. Similarly, cancers and polyps of PJS folks could be checked for APC2 mutation to determine if it's a factor for us.

One strange science note: I don't know how researchers found the APC2 locus since they weren't working from blood or tissue from FAP folks. They did analyze many cancers to determine LOH at the APC2 locus.

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