Cholangiocarcinoma (CCA) – cancer of the bile ducts – is associated with a chronic infection with the oriental liver fluke, *Opisthorchis viverrini*. Despite being the only eukaryotic organism that is designated as a ‘class I carcinogen’ by the International Agency for Research on Cancer (IARC), little is known about the transcriptome and genome of this enigmatic parasite. Recently, a gene discovery project for *O. viverrini* using the expressed sequence tag (EST) approach was begun (Laha et al 2007 *BMC Genomics* 8: 189). Among other genes, ESTs representing putatively secreted or transmembrane proteins with known roles in tumor induction and progression were identified, and these might play roles in the pathogenesis of *O. viverrini*-induced CCA. Here we discuss the preliminary characterization of three of these secreted or transmembrane proteins, orthologues of caspase 9, TGF-β receptor, and fibroblast growth factor receptor substrate 2 (FRS2). Caspase 9 is the apical caspase of the intrinsic pathway of apoptosis. The open reading frame (ORF) of the *O. viverrini* caspase 9 orthologue encodes a protease of 372 amino acid (aa) residues, with a NH2-terminal caspase recruitment domain (CARD) and COOH-terminal caspase 1L-1β converting enzyme domain (CRSe). Blast analysis revealed that its closest relatives were caspase 9 from *Gallus gallus* and *Xenopus laevis*. The TGF-β receptor orthologue includes a well-conserved catalytic domain common to serine/threonine kinases, involved in regulation of cell proliferation and differentiation. Phylogenetic analysis targeting the catalytic domain revealed close identity to TGF-β from *Echinococcus multilocularis* and the quail, *Coturnix coturnix*. The orthologue of *O. viverrini* FRS2 encoded an ORF of 296 aa with close phylogenetic identity to proteins of *Schistosoma japonicum* and *X. laevis*. FRS2 is a docking protein that transmits extracellular signals from the FGF receptor to a protein kinase signaling cascade. Recombinant forms of *O. viverrini* caspase 9 and FRS2 have been produced in *Escherichia coli* and purified by affinity chromatography. Ongoing studies with these antigens include investigation into their roles in signal transduction in the host-parasite relationship, their natural substrates, tissue localization, and mitogenicity, all of which may contribute to cholangiocarcinogenesis.