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(54) **Title**: COMPOSITIONS TARGETING THE SOLUBLE EXTRACELLULAR DOMAIN OF E-CADHERIN AND RELATED METHODS FOR CANCER THERAPY

(57) **Abstract**: The present invention is based, in part, on our discovery that targeting epitopes within one or more of the EC2-EC5 subdomains of E-cadherin results in the death of epithelial -derived tumor cells but not in the death of normal, healthy epithelial cells or non-epithelial cells including endothelial cells and fibroblasts. Accordingly, the compositions of the invention include polypeptides having an amino acid sequence of one or more of the EC2-EC5 subdomains of E-cadherin and biologically active variants thereof; expression vectors and cells for expressing such polypeptides; and agents (e.g., antibodies) that target the EC2-EC5 subdomains. The methods of the invention include methods of identifying and producing polypeptides having an amino acid sequence of one or more of the EC2-EC5 subdomains of E-cadherin or a biologically active variant thereof; methods of generating agents, such as antibodies, that target these polypeptides; and methods of administering such agents or eliciting their production in vivo to treat epithelial cancers or reduce the risk of their occurrence or recurrence.