E-cadherin is classified as a major tumour suppressor molecule and is the causing gene of Hereditary Diffuse Gastric Cancer (HDGC). E-cadherin loss of expression has a major impact in cell-cell interactions strength awarding cells with invasive abilities. Still, the molecular mechanisms underlying the aetiology of invasive carcinomas with E-cadherin loss are far from understood. As a model system we use HDGC associated germline missense mutations of the E-cadherin gene to unravel the underlying molecular mechanism of such highly invasive and mortal cancer syndrome. Herein, we will present how E-cadherin dysfunction leads to alterations in epithelial architecture and regulates cell signalling, ultimately promoting cell-matrix interactions and cell migration, which are key steps of the invasive process.