Year	Milestone	Publications
1995	Genetic Research begins	
1998	Identification of first inherited CDH1 mutations	Guilford, P., Hopkins, J., Harraway, J., McLeod, M., McLeod, N., Harawira, P., Taite, H., Scoular, R., Miller, A. and Reeve, A.E. E-cadherin mutations in familial gastric cancer. Nature, 392, 402-405 (1998). Guilford, P.J., Hopkins, J.B.W., Grady, W.M., Markowitz, S.D., Willis, J., Lynch, H., Rajput, A, Wiesner, G.L., Lindor, N.M., Burgart, L.J., Toro, T.T., Lee, D., Limacher, J-M., Shaw, D.W., Findlay, M.P.N. and Reeve, A.E. E-cadherin germline mutations define an inherited cancer syndrome dominated by diffuse gastric cancer. Human Mutation, 14, 249-255 (1999).
	HDGC pathology clarified	Grady, W.M., Willis, J., Guilford, P.J., Dunbier, A.K., Toro, T.T., Lynch, H., Wiesner, G., Ferguson, K., Eng, C., Park, J-G., Kim, S-J. & Markowitz, S. (2000). Methylation of the CDH1 promoter as the second genetic hit in hereditary diffuse gastric cancer. Nature Genetics, 26, 16-17. Charlton, A., Blair, V., Shaw, D., Parry, S., Guilford, P and Martin I.G. (2004). Hereditary diffuse gastric cancer: predominance of multiple foci of signet ring cell carcinoma in distal stomach and transitional zone. Gut, 53, 814-820 Humar, B., Fukuzawa, R., Blair, V., Dunbier, A., More, H., Charlton, A., Yang, H-K., Kim, W-H, Reeve, A.E., Martin, I. and Guilford, P. (2007). Destabilized adhesion in the gastric proliferative zone and c-src kinase activation mark the development of early diffuse gastric cancer. Cancer Res, 67, 2480-2489. Humar, B; Blair, V; Charlton, A; More, H; Martin, I, Guilford, P. E-cadherin deficiency initiates gastric signet-ring cell carcinoma in mice and man. (2009). Cancer Res. 69, 2050-6.
	Cell line models of HDGC developed	Chen, A., Beetham, H., Telford, B., Black, M., Priya, R., Wiggins, G., Guest, J., Godwin, T., Yap, A. and Guilford, P. (2014). E-cadherin loss promotes altered cytoskeletal organisation and disrupted adhesion but is insufficient for malignancy. BMC Cancer 14, 552-565.
2015	Genetic library screened	Telford, B., Chen, A., Beetham, H., Frick, J., Brew, T., Gould, C., Single, A., Godwin, T., Simpson, K. and Guilford, P. (2015). Synthetic lethal screens identify vulnerabilities in GPCR signalling and cytoskeletal organization in E-cadherin-deficient cells. Mol Cancer Ther. 14, 1213-1223.
	Drug libraries screened	Single A., Beetham H., Telford, B., Guilford, P. and Chen, A. A Comparison of Real-Time and Endpoint Cell Viability Assays for Improved Synthetic Lethal Drug Validation (2015). J Biomol Screen. 20, 1286-93. Godwin, T., Kelly, S., Brew, T., Single, A., Stylianou, C., Bougen-Zhukov, N., Currie.S., Telford, B., Beetham, H., Chen, A., Black, M. and Guilford, P. E-cadherin-deficient cells have synthetic lethal vulnerabilities in plasma membrane organisation, dynamics and function (2019). Gastric Cancer, 22, 273-286. Beetham, H., Chen, A., Telford, B., Single, A., Lackovic, K., Luxenburger, A. and Guilford, P. A high-throughput screen to identify novel synthetic lethal compounds for the treatment of E-cadherin-deficient cells (2019). Scientific Reports, 9, 12511-. Luxenburger, A., Bougen-Zhukov, N., Fraser, M., Beetham, H., Harris, L., Schmidt, D., Cameron, S., Guilford, P., Evans, G. Discovery of AL-GDa62 as a potential synthetic lethal lead for the treatment of gastric cancer (2021). J Med. Chem. (64), 18,114-18,142.
	Organoid models established	Bougen-Zhukov, N., Nouri, Y., Godwin, T., Taylor, M., Hakkaart, C., Single, A., Brew T., Permina E., Chen, A., Black, M and Guilford, P. Allosteric AKT inhibitors target synthetic lethal vulnerabilities in E-cadherin-deficient cells. Cancers, doi: 10.3390/cancers11091359 (2019).
	Candidate drugs validated in organoid models	Brew, T., Bougen-Zhukov, N., Schulpen, E., Decourtye, L., Nouri, Y., Godwin, T. and Guilford, P. Loss of E-cadherin leads to druggable vulnerabilities in sphingolipid metabolism and vesicle trafficking (2022). Cancers 14, 102. Decourtye-Espiard, L., Bougen-Zhukov, N., Godwin, T., Brew, T., Schulpen, E., Black, M.A. and Guilford, P. (2022). E-cadherin-deficient epithelial cells are sensitive to HDAC inhibitors. Cancers, 14, 175. Bougen-Zhukov, N., Decourte-Espiard, L., Mitchell, W., Redpath., Perkinson, J., Godwin, T., Black, M.A. and Guilford, P. (2022). E-cadherin-deficient cells are sensitive to the multikinase inhibitor dasatinib. Cancers, 14(1):175.