Epidemiological research has demonstrated that red meat consumption contributes to colorectal cancer (CRC) risk. The main hypothesis; the heme hypothesis, states that the ingestion of heme iron, which is more abundant in red compared to white meat, stimulates the formation of N-nitroso compounds (NOCs) and lipid peroxidation products (LPOs). Both NOCs and LPOs can exert geno- as well as cytotoxic effects, hence contributing to carcinogenesis. In this study, beef (model for red meat) and chicken (model for white meat) were digested in vitro (static model) as well as in vivo (Sprague-Dawley rats) to investigate gastrointestinal DNA adduct formation upon red vs. white meat digestion. DNA adduct formation was assessed by means of a state-of-the-art UHPLC-HRMS DNA adductomics platform, after which univariate (e.g. t-test) as well as multivariate (e.g. OPLS-DA) statistics were employed for red meat associated DNA adduct marker discovery. Combining the results from 3 independent in vitro and 1 in vivo digestion experiment(s), 7 DNA adduct types, including O6-carboxymethylguanine, dimethyl- or ethylthymine, methylguanine, heptanalguanine, a malondialdehyde-guanine adduct, and a malondialdehyde-cytosine adduct could be singled out as potential red meat digestion markers. This is highly relevant to the red meat-CRC hypothesis because the formation of the retrieved DNA adduct types may be linked to DNA alkylation and/or oxidation by e.g. NOCs and/or LPOs. Follow-up research will focus on the role of DNA adduct formation in the red meat-CRC pathway, as well as the mutagenic potential and human in vivo relevance of the proposed DNA adduct markers.