Background Colorectal cancer (CRC) is the second leading cause of cancer death worldwide, and more than 1/3 of all cases are rectal cancer. The standard neoadjuvant radiochemotherapy for locally advanced rectal cancer fails to benefit all patients due to individualize sensitivity to radiotherapy. It’s critical to understand the molecular mechanisms underlying pathological complete regression (pCR) in some patients.

Methods We collected 67 patients with rectal cancer who were treated with long-term radiotherapy and capecitabine chemotherapy from two hospitals. Among them, a total of 58 cases with both pre-treatment endoscopic biopsy specimens and surgical pathological sections available were picked procured and reassessed for Tumor Regression Grade (TRG) after treatment mentioned above. Formalin-fixed paraffin-embedded (FFPE) tissue samples from each individual were collected with two biological replicates. All the samples were processed by Pressure Cycling Technology coupled with Data-Independent Acquisition mass spectrometry for ples were processed by Pressure Cycling Technology coupled were collected with two biological replicates. All the sam-

Results A total of 6483 proteins are quantified with high confidence with a high Pearson correlation ($R^2=0.98$). Fifty-eight patients were divided into two groups according to the pCR condition after neoadjuvant radiochemotherapy. At the threshold of the adjusted p-value of 0.05 and fold change of > 1.5, we identified 127 up-regulated proteins and 205 down-regulated proteins in the pCR group. The former proteins were mainly involved in immune response and cell activation, while the latter mostly participated in metabolic processes. TIMER algorithm suggested a higher degree of immune infiltrates and their correlation with CDH11 were estimated by TIMER algorithm.

Conclusions Based on the proteomic analysis of biopsy specimens before neoadjuvant therapy, immune activation was identified as the potential mechanism via which some rectal cancer patients attained pCR.