Prediction of response to preoperative chemoradiotherapy in rectal cancer by multiplex kinase activity profiling

**Study Design**

In a phase II clinical trial 67 Locally Advanced Rectal Cancer (LARC) patients were treated with a chemoradiation therapy (CRT) regimen consisting of radiotherapy, fluorouracil, and where possible, oxaliplatin. Pretreatment tumor biopsy specimens were analyzed using PamChip® microarrays with kinase peptide substrates, and the resulting substrate phosphorylation profiles were correlated with tumor response to preoperative treatment as assessed by histomorphologic tumor regression grade (TRG) (figure 1). A predictive model for TRG scores from phosphosubstrate signatures was obtained by partial-least-squares discriminant analysis. Prediction performance was evaluated by leave-one-out cross-validation and use of an independent test set (figure 2).

**Key Findings**

Of the 67 patients, 73% and 15% were scored as good responders (TRG 1–2) or intermediate responders (TRG 3), and 12% were poor responders (TRG 4–5). In a testset of 7 poor responders and 12 good responders, treatment outcome was correctly predicted for 95%. Application of this testset model on the remaining 48 patient samples resulted in correct prediction for 85%. (Folkvord 2010)

**"Author Quote"**

Although skeptical at first we became convinced that kinase activity profiling may help predict response to preoperative radiotherapy in LARC.

**Background**

Locally advanced rectal cancer (LARC) comprises tumors that have grown through the rectal wall to an extent that precludes complete surgical resection and the achievement of adequate circumferential resection margin. A key objective of preoperative chemoradiotherapy (CRT) is macroscopic downstaging and control of subclinical tumor extension within the pelvic cavity, enabling complete tumor clearance after surgery.

**Conclusion**

Multiplex kinase activity profiling may identify functional biomarkers predictive of tumor response to preoperative CRT in LARC.

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**References:**