Molecular Profiling of Lung and Colorectal Cancer: Added Value of Next Generation Sequencing

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Background and objectives

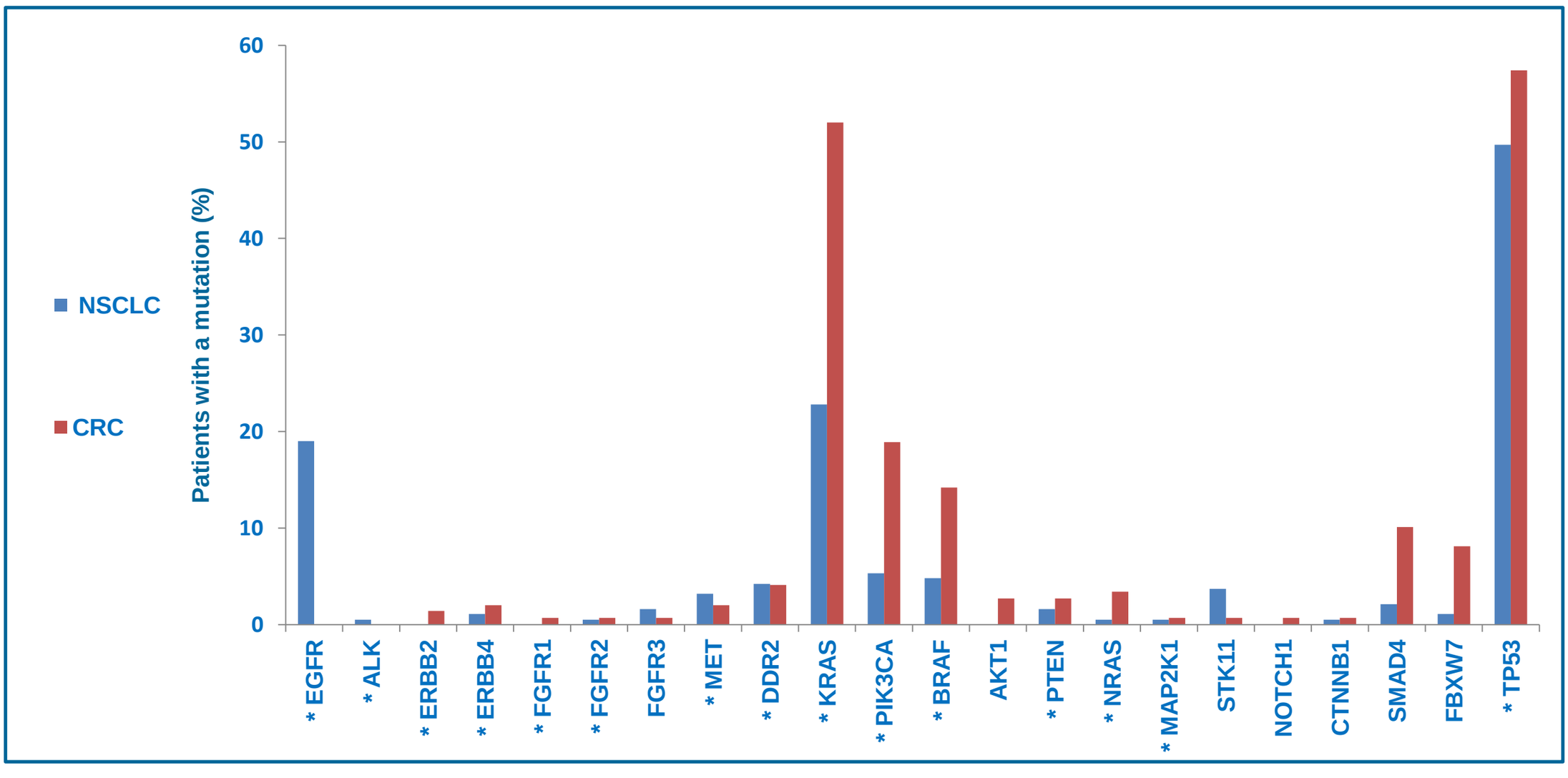
The results of DNA and RNA molecular profiles obtained from non-small cell lung cancer (NSCLC) and colorectal patients (CRC) since the implementation of a Next Generation Sequencing (NGS) panel in a diagnostic laboratory setting were analyzed. A review of the detected mutations in its clinicopathological context was performed and the hypothetical increased number of patients suitable for a targeted therapy was tested.

Methods

The series included 364 formalin-fixed paraffin-embedded tumors corresponding to 211 patients with NSCLC and 153 patients with CRC. DNA was extracted and libraries were prepared with a 22 gene panel (EGFR, ALK, ERBB2, ERBB4, FGFR1, FGFR2, FGFR3, MET, DDR2, KRAS, PIK3CA, BRAF, AKT1, PTEN, NRAS, MAP2K1, STK11, NOTCH1, CTNNB1, SMAD4, FBXW7 and TP53) from 10ng of DNA (Oncomine Solid Tumour DNA. ThermoFisher). Only NSCLC were tested with a RNA NGS panel for rearrangements in 4 genes: ALK, ROS1, RET and NTRK1 (Oncomine Solid Tumour Fusion Transcript. ThermoFisher). Templates were prepared with an Ion Chef System and sequencing performed in an Ion Personal Genome Machine (PGM) System. Data were analyzed with PGM Torrent Server 5.6.20, IonReporter 5.6 and IonTorrent Oncomine Knowledgbase Reporter (ThermoFisher Scientific software). The Mean Coverage was greater than 500X in all samples warranting a sensitivity higher than 2,5%.

Results

In NSCLC, 235 mutations were detected. Mutations in EGFR (19%), KRAS (22,8%), TP53 (49,7%) and, ranging from 0,5% to 6%, in ALK, ERBB4, FGFR2, FGFR3, MET, DDR2, PIK3CA, BRAF, PTEN, NRAS, MAP2K1, STK11, CTNNB1, SMAD4 and FBXW7 were detected. At a RNA level the 3,5%, 1,4% and 2,1% of NSCLC showed an ALK, ROS1 and RET rearrangement respectively. No NTRK1 alteration was detected. In CRC, 272 mutations were detected. Mutations in KRAS, NRAS, BRAF, TP53, PIK3CA, SMAD4 and FBXW7 were detected in 52%, 3,4%, 14,2%, 57,4%, 18,9%, 10,1% and 8,1% of patients, respectively. Moreover, mutations in ERBB2, ERBB4, FGFR1, FGFR2, FGFR3, MET, DDR2, AKT1, PTEN, MAP2K1, STK11, NOTCH1 and CTNNB1, ranging from 0,7% to 5%, were detected (Figure 1). Most of these mutations would have not been detected with molecular techniques used before the implementation of NGS.



Conclusion

Molecular profiling by NGS increases over 50% the NSCLC and CRC patients suitable for a targeted therapy and also provides significant prognostic information.

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