Supplementary Methods

Array Comparative Genomic Hybridization

DNA was isolated from 10 frozen tumor specimens and labeled using the Agilent Genomic DNA Enzymatic Labeling Kit (Agilent Technologies, Santa Clara, CA) following manufacturer's protocols (version 5.0) with 2 μg of starting material. The samples were hybridized to the high-resolution Agilent Human Genome 244K 60-mer oligonucleotide CGH-arrays containing ~240 000 probes. The hybridizations were conducted in hybridization chambers at 65℃ for 40 hours at 20rpm, then washed, dried and were scanned on the Agilent DNA Microarray Scanner (G2565BA) at 5 um, with 100% PMT for both green and red lasers. The resulting tiff image was quantified and normalized using Agilent Feature Extraction Software version 9.5.3.1 using the CGH-v4_95_Feb07 protocol.

Fluorescence *in situ* Hybridization

The slides were baked overnight at 56^{o}C. The following day, the slides were de-waxed in xylene and dehydrated in 100% ethanol. After dehydration the slides were digested with pepsin (Sigma-Aldrich) prior to co-denaturation at 80^{o}C and hybridization overnight at 37^{o}C with the commercially available *EGFR/CEP7* probe cocktail (Abbott Molecular). The following day, the slides were processed in a wash of 0.3% NP-40/ 0.4X SSC for 2 min at 72^{o}C and a wash of 0.1%NP-40/2X SSC for 5 min at RT. The slides were rinsed in 1X PBS, mounted in a DAPI/Antifade medium (Vectashield/Vector Laboratories), and visualized at 60X with a Zeiss Axioskop fluorescence microscope (Carl Zeiss Canada). At least 50 nuclei were enumerated for both *EGFR* and *CEP7* signals for each core.

Gene-specific Methylation Analysis

Methylation changes for candidate genes were assessed using matched 'Level 3' TCGA ccRCC methylation data generated by Illumina Infinium HumanMethylation450 and HumanMethylation27 arrays. A probe was considered significantly methylated if a) it had a β-value difference of ± 0.2 between tumor and normal kidney (hypermethylation (> 0.2) or hypomethylation (< - 0.2)) and b) met the β-value threshold in at least 5% of cases for either hypermethylation or hypomethylation. Frequency of methylation changes was assessed according to combined matching significantly methylated probes in the HumanMethylation450 and HumanMethylation27 arrays.