Figure S1. Schematic design for this study. PC-9 cells in three environments were induced to resistance to gefitinib by increasing treatment does step by step. In Mr group, PC-9 cells were always co-cultured with macrophages derived from THP-1 in either gefitinib treatment or recovery process. In Mm group, PC-9 cell were treated with gefitinib alone, while recover in co-culture with macrophages derived from THP-1. In control group, PC-9 cells were not co-cultured with THP-1 during the whole induction process. Mr, resident macrophage; Mm, migrated macrophage.

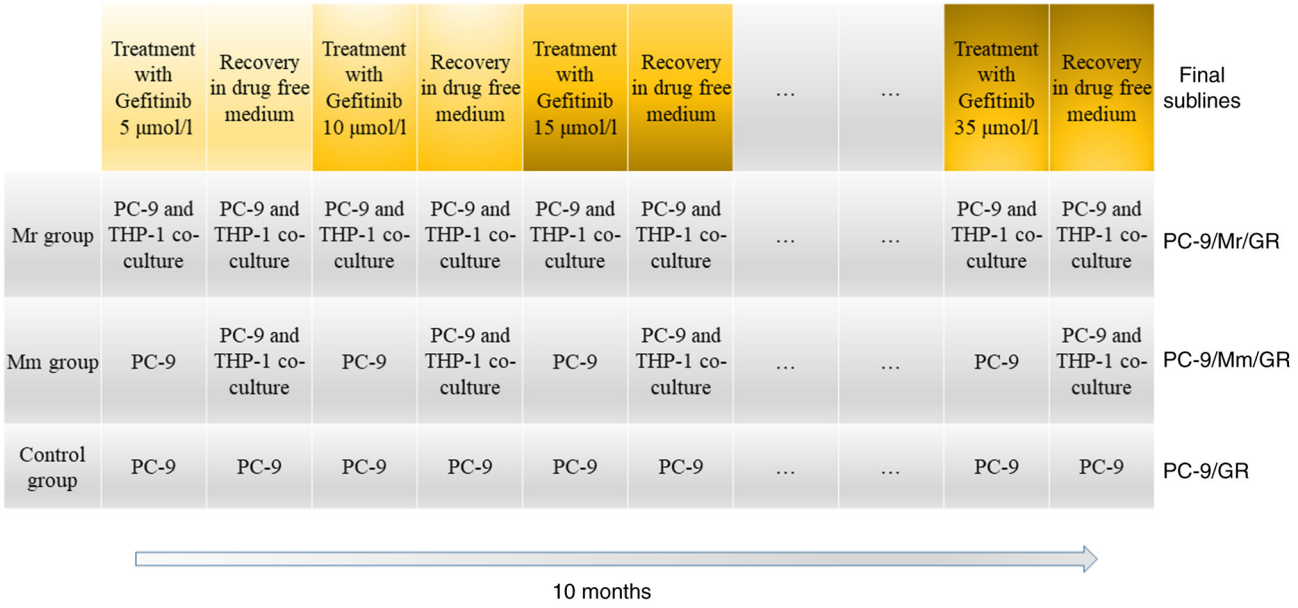

Figure S2. Hot spot mutations in EGFR exon 18-21 detected using high-resolution melting analysis. Normalized melting curves of EGFR exon 18-21 fragments were shown. Resistant sublines (PC-9/Mm/GR, PC-9/Mr/GR and PC-9/GR) had the same genotype with PC-9 cells in these fragments. No new mutations were found, and all of them displayed exon 19 deletion mutation. Mr, resident macrophage; Mm, migrated macrophage.

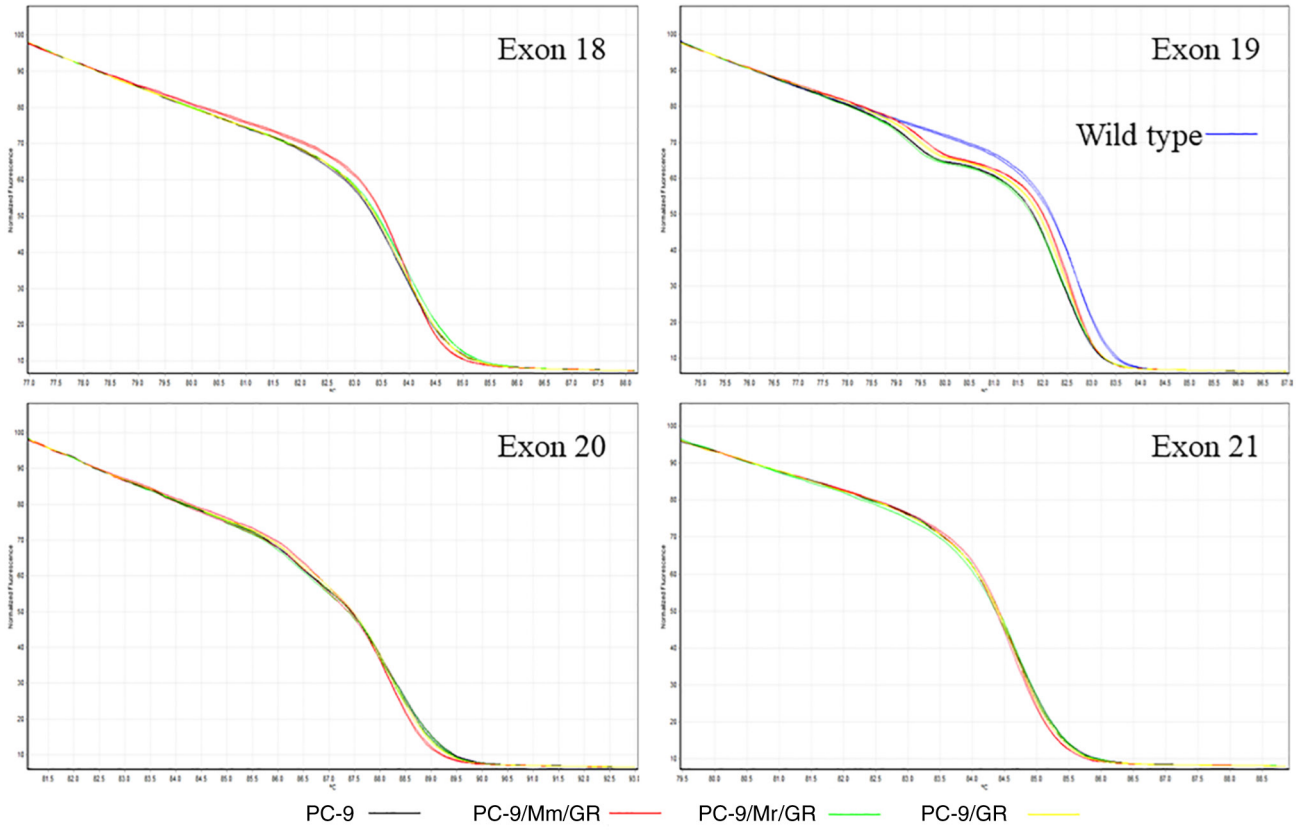

Figure S3. EGFR exon 18-21 fragments sequencing results. PC-9 cells and resistant sublines (PC-9/Mm/GR, PC-9/Mr/GR and PC-9/GR) showed the same sequencing results. Exon 18, 20 and 21 fragments were wild-type (hot spot amino acids and codons were marked). There was a deleted mutation in exon 19 (c.2235_2249delGGAATTAAGAGAAGC, E746-A750 del, ENST00000275493.7). Amino acids 744I, 751T and codons in wild type were marked.

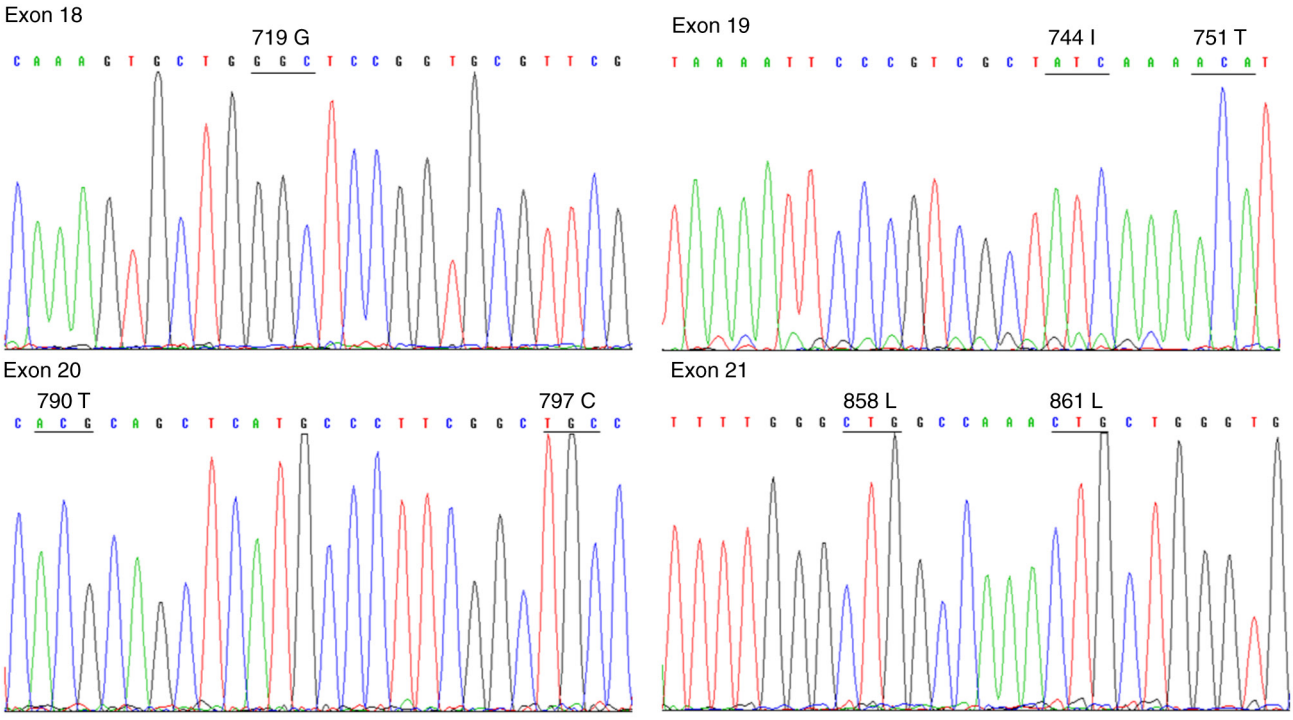

Figure S4. E-cadherin and vimentin expression with immunofluorescence. E-cadherin (green) and vimentin (red) expression in (A and B) PC-9, (C and D) PC-9/GR, (E and F) PC-9/Mm/GR and (G and H) PC-9/Mr/GR.