Ioncopy: a novel method for calling copy number alterations in amplicon sequencing data including significance assessment.

Recently, it has been demonstrated that calling of copy number alterations (CNAs) from amplicon sequencing (AS) data is feasible. Most approaches, however, require non-tumor (germline) DNA for data normalization. Here, we present the method Ioncopy for CNA detection which requires no normal controls and includes a significance assessment for each detected alteration. Ioncopy was evaluated in a cohort of 184 clinically annotated breast carcinomas. A total number of 252 amplifications were detected, of which 183 (72.6%) could be validated by a call of an additional amplicon interrogating the same gene. Moreover, a total number of 33 deletions were found, whereof 27 (81.8%) could be validated. Analyzing the 16 most frequently amplified genes, validation rates of over 89% could be achieved for 11 of these genes. 11 of the top 16 genes showed significant overexpression in the amplified tumors. 89.5% of the HER2-amplified tumors were GRB7 and STARD3 co-amplified, whereas 68.4% of the HER2-amplified tumors had additional MED1 amplifications. Correlations between CNAs measured by amplicons in HER2 exons 19, 20 and 21 were strong (all R > 0.93). AS based detection of HER2 amplifications had a sensitivity of
90.0% and a specificity of 98.8% compared to the gold standard of HER2 immunohistochemistry combined with in situ hybridization. In summary, we developed and validated a novel method for detection and significance assessment of CNAs in amplicon sequencing data. Using Ioncopy, AS offers a straightforward and efficient approach to simultaneously analyze gene amplifications and gene deletions together with simple somatic mutations in a single assay.

Zeitschriftentitel / Abkürzung:
Oncotarget

Jahr:
2016

Band:
7

Heft / Issue:
11

Seiten:
13236-47

Sprache:
eng

Volltext / DOI:
http://doi.org/10.18632/oncotarget.7451

Pubmed:

TUM Einrichtung:
Institut für Allgemeine Pathologie und pathologische Anatomie

Occurences:
- Hochschulbibliographie > 2016 > Fakultäten > Medizin > Institut für Allgemeine Pathologie und Pathologische Anatomie
- Einrichtungen > Fakultäten > Fakultät für Medizin > Kliniken und Institute > Institut für Allgemeine Pathologie und Pathologische Anatomie > 2016

entries: