Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
Methods: Xmal-RRBS dataset for 34 TNBC biopsies taken prior to NAC was used. Virtual amplicons were designed under the following criteria: at least two MSRE (BstHII and/or HpaII) recognition sites within the amplicon, the amplicon length no more than 100 bp to provide high MSRE-qPCR efficiency, the average difference in the methylation level between adjacent CpG pairs no more than 10%. To select amplicons, MSRE sites were hierarchically clustered with the distance metric of physical distance over the genome and the difference in their methylation level, followed by complete-linkage agglomeration to prevent lengthening of amplicons via chaining phenomenon. Diagnostic potential was assessed with cross-validated AUC. Markers with AUC > 75% were selected to form panels.

Results: Genes APCDD1L, RUSC1-AS1, MYO15B, EXOC2, THBS2, MXRA5, ANKRD64 were selected to form possible combinations of markers. Eventually, 120 combinations of amplicons panels that discriminate NAC response were obtained and top-10 are shown in the table.

| Panels | AUC, % | Sensitivity, % | Specificity, % | Accuracy, % |
|--------|--------|----------------|----------------|-------------|
| RUSC1-AS1, MYO15B, ANKRD46 | 91 | 89 | 83 | 85 |
| APCDD1L, RUSC1-AS1 | 88 | 96 | 61 | 77 |
| RUSC1-AS1, MYO15B, MXRA5, ANKRD46 | 88 | 82 | 85 | 84 |
| APCDD1L, RUSC1-AS1, MYO15B | 88 | 81 | 81 | 81 |
| APCDD1L, RUSC1-AS1, ANKRD46 | 88 | 93 | 69 | 80 |
| RUSC1-AS1, MYO15B, THBS2, ANKRD46 | 87 | 81 | 84 | 82 |
| APCDD1L, RUSC1-AS1, THBS2 | 87 | 89 | 65 | 76 |
| APCDD1L, MYO15B, THBS2 | 87 | 77 | 88 | 83 |
| RUSC1-AS1, THBS2, MXRA5, ANKRD46 | 86 | 82 | 82 | 82 |
| RUSC1-AS1, EXOC2 | 86 | 76 | 88 | 83 |

Conclusions: Our approach shows promising results for designing multiplex MSRE-qPCR panels to accurately predict TNBC response to NAC. Further verification of its efficacy is required on validation cohorts.

Legal entity responsible for the study: Research Centre for Medical Genetics, Moscow, Russia.

Funding: The research was supported by Russian Science Foundation (project No 18-15-00430).

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.08.784

### 1144P When Al-based image analysis gets in clinical trials

P. Mésange1, M. Bonnet2, J. Deen3

1APH Department, Covance Central Laboratory Services SA, Meyrin, Switzerland; 2Histology, Covance Central Laboratory Services SA, Meyrin, Switzerland; 3Histology, Covance, Geneva, Switzerland

Background: Especially during the COVID-19 pandemic, implementation and development of whole slide scanning lead to an active growth of digital pathology and image analysis (IA). In the present study, we retrospectively conducted a global evaluation of three Breast cancer markers: ER, PR and Ki67 with the aim to study the correlation between pathologist conventional semi quantitative scoring method on glass and scanned slides versus artificial intelligence-based IA.

Methods: Study samples were scored independently either by five independent pathologists on scanned images and glass slides, or using supervised IA algorithms (IA results were validated by pathologists). The readout for the three markers was the percentage of tumor positives stained cells. The correlation between the pathologist evaluation on glass slides versus scanned images was calculated using Pearson's correlation coefficient. Pathologist's evaluations and IA results were compared using Intraclass Correlation Coefficient (ICC). Additionally, the average time spent by the pathologist per sample was measured for each evaluation method.

Results: The correlation of pathologist evaluation between glass slide and scanned image showed a Pearson's correlation coefficient ≥ 0.90 for each marker. The ICC between IA algorithm and pathologist was on average over 0.8 for the three markers, showing a good agreement between the different scoring method. However, some challenges were identified related to the detection of tumor area that needed some additional pathologist review for specimen. The average time spent by the pathologist per sample was at least 10 minutes.

Conclusions: Based on the Pearson's correlation coefficient and the ICC results, we observe an equivalence in the pathologist conventional scoring (Image or glass slides) and the use of IA. In an era where regulations are still being discussed for the use of algorithms by the FDA (Al-based or not), we can mitigate regulatory requirements by having pathologists reviewing the results of a digital analysis. We conclude here to a benefit from the combination of pathologist evaluation and IA in terms of time with at least equivalent results in terms of accuracy.

Legal entity responsible for the study: Covance.

Funding: Has not received any funding.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.08.785

### 1144P Reliable detection of BRCA1 and BRCA2 large genomic rearrangements in FFPE tissue: A new diagnostic benchmark for somatic BRCA testing

N. Valtcheva1, B.D. Nguyen1, U. Freiberger2, Z. Varga3, C. Britschgi3, K.J. Dedes4, M. Rechsteiner1

1Department of Pathology and Molecular Pathology, University Hospital Zurich - Institute of Pathology, Zurich, Switzerland; 2Department of Gynecology, University Hospital Zurich, Zurich, Switzerland; 3Department of Medical Oncology and Hematology, USZ - University Hospital Zurich, Zurich, Switzerland

Background: PARP inhibitors are used for treatment of tumors lacking function of the double-strand DNA break repair proteins BRCA1 or BRCA2 and are already approved for several cancer types. Thus, it is clinically crucial to determine germline as well as somatic BRCA1/2 mutations in these patients. The amplicon-based Oncomine BRCA1 and BRCA2 Assay is a test routinely used in diagnostics with FFPE specimens. The assay is validated for the detection of mutations, however, data on its performance in detecting large genomic rearrangements in FFPE tissue, is scarce.

Methods: We cross-validated Oncomine BRCA1 and BRCA2 Assay in blood samples and/or FFPE tissue with multiplex ligation-dependent probe amplification (MLPA) for exon deletions and OncoScan, and an in-house hybridization-based target capture NGS assay (MelArray) with a customized pipeline for the detection of loss of heterozygosity (LOH) and heterozygous versus complete gene loss.

Results: The Oncomine BRCA1 and BRCA2 Assay could detect both exon deletion and mono- and bi-allelic losses of the BRCA1/2 genes in samples with tumor content greater than 40%. We show that the therapeutically relevant large genomic rearrangements are reliably detected with the amplicon-based Oncomine BRCA1 and BRCA2 Assay in FFPE tumor tissue.

Conclusions: Based on our data, we suggest somatic BRCA testing as standard diagnostic prescreening prior to germline BRCA testing. Thus, a rapid, reliable and affordable SBRA testing could be used in the future as standard analysis after diagnosis with ovarian, breast, pancreatic and prostate cancer in routine diagnostics. This will immensely shorten the time for treatment decision, especially for patients without BRCA1/2 alterations since generally only patients with SBRA mutations will be referred to the more time consuming genetic counselling and germline (gBRA) testing.

Legal entity responsible for the study: University Hospital Zurich.

Funding: Innovation Pool of the University Hospital Zurich # INOV00102.

Disclosure: All authors have declared no conflicts of interest.

https://doi.org/10.1016/j.annonc.2021.08.786

### 1144P Closing the target gap: A computational approach to optimizing therapeutic selection for cancer patients

M. Grushko1, J. Goldstein, Z. ElSeht, A. Alarcon, N. Jones, M. Samizadeh, Y. Zhu, J. Kaplan, K. Arline

1Delve, Shepherd Therapeutics, Natick, MA, USA

Background: While significant progress has been made in developing new therapies for cancer patients, many patients lack treatments that result in favorable outcomes. Existing patient-therapy matching algorithms frequently rely on mutations or other well-studied targets for which limited FDA-approved therapies exist. In contrast, SHEPHERD's approach, called DELVE, uses computational and mathematical tools informed by transcriptomic data to match therapies with the models, cancers, and specific patients that will be most impacted by drug treatment, regardless of mutational status.

Methods: DELVE leverages bioinformatics, chemoinformatics, proprietary algorithms, deep learning neural networks, random forest classifiers, and other tools to generate transcriptomic-level drug response-resistance signatures. DELVE was deployed to characterize drug response and resistance across thousands of in vivo, ex vivo, and in vitro cancer models and over 75,000 patient samples representing 125 cancers and healthy tissues.

Results: DELVE was able to correctly classify the highest and lowest responding drug-cell line pairs with 96% sensitivity [CI 95% 0.93-0.96] and 88% specificity [CI 95% 0.80-0.92].