

DRAGEN v3.10.10

Software Release Notes

Introduction

These release notes detail the key changes to software components for the Illumina® DRAGEN™ Bio-IT Platform v3.10.10.

Changes are relative to DRAGEN™ v3.10.9. If you are upgrading from a version prior to DRAGEN™ v3.10.9, please review the release notes for a list of features and bug fixes introduced in subsequent versions.

DRAGEN™ Installers, User Guide and Release Notes are available here:

https://support.illumina.com/sequencing/sequencing_software/dragen-bio-it-platform.html

The 3.10.10 software package includes installers for the on-site server:

- DRAGEN™ SW Intel Centos 7 - dragen-3.10.10-8.el7.x86_64.run
- DRAGEN™ SW Intel Oracle 8 - dragen-3.10.10-8.el8.x86_64.run

The following configurations are also available on request:

- Amazon Machine Image (AMI)
- Microsoft Azure Image (VM)
- RPM packages for Centos 7 for Amazon Web Services (AWS)

Deprecated platforms:

- Support for DRAGEN Server v1 FPGA cards has been deprecated since DRAGEN™ v3.10
- Support for Ubuntu has been deprecated since DRAGEN™ v3.9
- Support for Intel CentOS 6 has been deprecated since DRAGEN™ v3.8

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Overview

Below is a summary of the changes included in this DRAGEN™ v3.10.10 patch release. This is a minor update.

Issues Resolved

Issues resolved on DRAGEN™ v3.10.10, compared to v3.10.9

Component/s	Defect ID	Description
Gvcf Genotyper	DRAGEN-16614	Fix a crash that is encountered due to tabix indexing while concatenation is enabled. The fix disables tabix during concatenation.
Coverage Metrics	DRAGEN-16386 SET-2665	Fix for abnormal coverage metrics. Since DRAGEN v3.8 the autosomal coverage calculated over a bed file could be incorrect, and sometimes abnormal (extremely large values).
scRNA	DRAGEN-16360 SET-2792	Fix for a hang on NextSeq2000 instrument, due to scRNA out-of-memory condition. The fix reduces the amount of memory used by the scRNA pipeline.
HWAL, BCL	DRAGEN-18618	Fix for error loading ZIP bitstream for DRAGEN BCL, when downgrading from DRAGEN v4.0. When a SW install transitions between versions, and a different ZIP FPGA bitstream is loaded than the version in the newly installed SW, the 3.x software did not correctly detect the installed version leading to crash.

Known Issues

Known issues of the DRAGEN™ v3.10.10 release

Component/s	Defect ID	Issue Description	Remedy / Workaround
SNV VC	DRAGEN-20618	DRAGEN SNV caller fails during NTD error estimation when there are 0 input reads	No workaround. When NTC samples are run, they sometimes contain zero reads, leading to crash in the SNP error estimation.
PhenoHRD	DRAGEN-20471	PhenoHRD error when running high tumor fraction LOH sample	No workaround. Very high tumor fraction samples can cause an error in LOH estimation
SV	DRAGEN-20127	PML-RARA fusion called as non-PASS even after contamination adjustment	Clinically actionable, orthogonally validated PML-RARA fusion in AML sample not called in tumour/normal analysis. Workaround: Tumour-in-normal contamination adjustment rescue the variant, but is non-PASS

Component/s	Defect ID	Issue Description	Remedy / Workaround
BCL	DRAGEN-20064	BCL convert aborts with an empty [BCLConvert_Data] section in v2 sample sheets	BCL convert aborts when there is empty [BCLConvert_Data] or [BCLConvert_Settings] sections in v2 sample sheets. Workaround, add entries to the sections.
Biomarkers, TMB	DRAGEN-20062	TMB accuracy failures in WES T/O	Nonsyn TMB metrics are not meeting requirements for Tumor-Only samples. No workaround
BOSS, Gene Fusion	DRAGEN-19957	DRAGEN Amplicon fails on an RNA sample	RNA samples may hang/fail when they are sequenced with extremely high depth. Workaround: Downsample to a reasonable depth. The added depth of excessive duplicates has no impact on accuracy
Nirvana, Somatic, BaseSpace	DRAGEN-19921	DRAGEN Somatic App – Redundant .annotated.json.gz files created with Nirvana enabled	Two identical files are produced. "hard-filtered.vcf.annotated.json.gz" and "hard-filtered.annotations.json.gz". One can be ignored.
SNV Somatic	DRAGEN-19389	Variants not normalized in VCF	No workaround. For non-UMI modes, low call threshold introduces multi allelic calls that are not being normalized in the VCF
BCL	DRAGEN-19323	BCL Strict Mode does not abort when *.bci lane file corrupted via truncation	No workaround. The strict mode check misses some input error modes.
BCL	DRAGEN-19292	BCL report fastq_list.csv contains incorrect file paths when ORA-interleaved compression format is used	No workaround. When "dragen-interleaved" compression format is used, the fastq_list.csv file contains two files (instead of one single interleaved file) under the "Read1File" and "Read2File" columns
API, Paralog Caller	DRAGEN-19244	RawBuffer2DbamTransformer causes hang on large number of alignments for same fragment	A hang on very high depth input when certain callers such as Paralog/CYP2D6/Expansion Hunter are run from BAM without map/align. The recommendation is to run these callers with map/align enabled.
Force GT	DRAGEN-19188	Aborted Dragen somatic analysis with FGT	No workaround. A crash has been observed on a somatic sample with Force GT enabled.
Trimming	DRAGEN-19075 SET-3449	Discrepancy of Adaptor Trimming between Fastq Toolkit and DRAGEN Fastq Toolkit	The commonly used 3' trimmers work as intended, but the hidden/rarely used 5' trimmers require their sequences be reversed.
GVCF, Nirvana, Somatic SNV	DRAGEN-18826	Tumor Only analysis with GVCF mode aborts in BSSH with memory issue	No workaround. System runs Out of Memory when large somatic sample (~120x) is run with TMB and VCF/GVCF annotation enable, due to

Component/s	Defect ID	Issue Description	Remedy / Workaround
			GVCF being loaded into memory for tagging.
BaseSpace	DRAGEN-18531	Downsampling does not allow expansion hunter launch when sample-sex is set to unknown	No workaround. Expansion Hunter requires a sample sex, user may not specify unknown. User can specify male/female or "auto" to autodetect. Downsampling does not work with "auto".
RNA VC, Force GT	DRAGEN-18375	Native Dragen RNA VC fails with EFATAL: Caught signal Segmentation fault (11)	No workaround. A segfault has been observed in Force GT when RNA sample is processed with Force GT enabled in the variant calling
SNV Somatic	DRAGEN-18272	DRAGEN VCF index file doesn't match tabix and won't work with tabix to parse using regions "chr1"	No workaround. DRAGEN GVCF can produce a tabix index that won't work with tabix tool.
RNA Alignment	DRAGEN-18224	RNA VC FP resulting from inappropriate duplicate marking	No workaround. Observed false positive RNA variant calls in low quality FFPE samples, due to an issue in duplicate marking.
Gene Fusion	DRAGEN-18069	FP fusion detected 3-bp away from another true breakpoint	No workaround. The system may produce a false fusion call that is 3-bp away from expected/true fusion call.
Gene Fusion	DRAGEN-17524	RNA fusion false positive due to polyG misalignment	No workaround. RNA fusion caller may produce false positive due to polyG misalignment
GVCF Genotyper	DRAGEN-17499	Empty msVCF output with whole contig gg-regions bed file	Empty output is produced when the gg-regions contain the whole chromosomes. Workaround is to drop whole regions from the regions bed file.
UMI	DRAGEN-17082	When UMI downsampled, BAM does not have SA tag	No workaround. When running DRAGEN from fastq with downsampling, UMI collapsed BAM does not have Supplementary alignments (or SA tag)
BCL	DRAGEN-17015	Incorrect Error Message for Missing BCL Input Directory	Ignore the incorrect error message when --bcl-input-dir is missing
Ora compression, UMI	DRAGEN-17533	Exception when using Ora inputs for map/align and Ora input for "---umi-source".	The "umi-source" option does not support Ora input. The workaround is to supply FASTQ file as "umi-source"
Downsampling, UMI	DRAGEN-17082	When downsampling is used with UMIs via "enable-downsampler=true", the BAM does not contain SA tags	No workaround. Issue is specific to the use case combination of UMI collapsing and use of down sampler.
BCL	DRAGEN-16555	Minimum Adapter Overlap setting not working	Whether it's set to a valid or invalid value, an error message is displayed. No workaround

Component/s	Defect ID	Issue Description	Remedy / Workaround
Infrastructure	DRAGEN-16498	AWS f1.4x LICENSE_MSG Challenge get token error: Get instance ID failed (Unable to retrieve AWS identity signature)	Timeout while retrieving AWS instance ID has been observed. The rate of occurrence has been too low to measure. This leads to failure in the licensing and dragen job exits, run fails. Re-run would pass
DNA Alignment	DRAGEN-16468	Bam generated from file conversion CRAM -> BAM with hg19_alt_masked_v2 reference has invalid header	Reproducible issue that has been shown to have existed since v3.7 or earlier. When converting from CRAM to BAM using dragen "file-conversion" method, the BAM has an invalid header due to a bug in the CRAM reader. No workaround. Re-header the file
DNA Alignment	DRAGEN-16467	Germline workflow is slower with graph hash table	Dragen run time is roughly 6.3% slower with graph aligner and graph reference is used, compared to non-graph. The increased run time is in both mapper and variant caller phases. No workaround
Dedup/UMI	DRAGEN-16412	Probabilistic UMI output is different from run to run	There is a run-run variation in the UMI probabilistic model. Non-prob model (non-random UMI) does not have run-to-run variation. The variation leads to ~2 reads being missing from output. This impact shall be a very small fraction.
DupMarking	DRAGEN-16399	Assertion `pos < m_num_bits' failed, in Dupmark:: DupmarkTable:: getDuplicates()	Crash in duplicate marking when there are more than 4G read pairs, which can happen when reads of multiple replicates are combined into one read group through manual BAM file editing. The system has a physical limit. Not a regression from prior releases
Cloud / Azure	DRAGEN-16335	popen exception on azure cloud suites	A very long running workflow such as TSO500 ctDNA crashes on Azure due to eventual failure in popen() calls. The issue is reproducible. No workaround
Somatic	DRAGEN-16319	Elevated SNP and INDEL FP on ICGC datasets	The impact of the issue is an elevated number of FPs for ICGC datasets in 3.10 compared to 3.9: a 5-6% increase in the SNP FPs and a 25%-30% increase in the INDEL FPs.
DNA Alignment	DRAGEN-16308	read trimmer adapter trimming sigabort during RecomputeTags:: computeTags	Reproducible when running different read trimmers back-back. Workaround to run dragen_reset

Component/s	Defect ID	Issue Description	Remedy / Workaround
Amplicon Gene Fusion	DRAGEN -16254	Excessive RNA Amplicon runtime on large samples	RNA Amplicon run time is very long when the coverage is significantly higher than expected for typical Amplicon samples
SNV VC Somatic	DRAGEN -16149	Germline MNV - phased calls with same PS and GT and within distance threshold are not getting combined into MNVs	Some phased calls are not getting combined into MNVs to MNV output. Full support for germline MNV is planned for a subsequent release
Metrics scRNA	DRAGEN -15950	A run-run variation in scRNA output	Some datasets have run-to-run variations in the mapping metrics Q30 metrics field. The issue affects only the metrics output and not the caller output
BCL	DRAGEN -15944	DRAGEN BCL logs insufficient warning when corrupt files supplied	In the rare event of a corrupt aggregated bcl. bgzf input file, the customer will correctly receive an error message of the lane and the cycle that is corrupted, but not the specific file name.
Methyl-Seq	DRAGEN -15796	md5sum discordance b/w cloud and local runs	Impacts multi-pass mode and specific dataset. Single pass mode has been the recommended mode and does not have the issue. Multi-pass will be deprecated in future.
DNA Alignment EH	DRAGEN -15151	Large run to run variation of mapper run time for EH	Up to 20% run time variation seen for mapper phase
HW GRAPH RNA VC	DRAGEN -13717	RNA VC hits ERROR: Invalid node flags	Issue is a HW graph error and rare (happens once every 6-9 months in routine VC testing). The assertion check / trap will remain in place so that invalid results will not be produced for end user. If seen in field, recommendation is to re-run sample as it is expected to pass.
Compression	DRAGEN -10783	BAM input to DNA mapper: Deflate engine error: 0x9080 on stream 1	Extremely low repeatability. A re-run will pass

SW Installation Procedure

- Download the desired installer from the Illumina support website and unzip the package
- The archive integrity can be checked using: `./<DRAGEN 3.10.9 .run file> --check`
- Install the appropriate release based on your Linux OS with the command: `sudo sh <DRAGEN 3.10.9 .run file>`
- Please follow the installer instructions. Server power cycle may be required after installation, depending on the currently installed version. If an updated FPGA shell image needs to load from flash, this is only achieved with power cycle.
 - A power cycle is required when upgrading from v3.3.7 or older
 - A power cycle is required when downgrading to v3.3.7 or older

- A power cycle is not required when upgrading from a release after v3.3.7
- Procedure to downgrade to v3.3.7 or older:
 - Requires the following three steps. The prior .mcs file needs to be flashed manually:
 - Install the prior release: `sudo sh <DRAGEN 3.3.7 .run file>`
 - `program_flash /opt/edico/bitstream/07*/*.mcs`
 - Power cycle