

DRAGEN v3.9.5

Software Release Notes

Introduction

These release notes detail the key changes to software components for the Illumina® DRAGEN™ Bio-IT Platform v3.9.5.

Changes are relative to DRAGEN™ v3.9.3. If you are upgrading from a version prior to DRAGEN™ v3.9.3, 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 3.9.5 software package includes:

- DRAGEN™ SW for x86 Centos 7 - dragen-3.9.5-8.el7.x86_64.run
- DRAGEN™ SW for x86 Oracle 8 - dragen-3.9.5-8.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 IBM PPC has been deprecated since DRAGEN™ v3.7
- Support for Intel CentOS 6 has been deprecated since DRAGEN™ v3.8
- Support for Ubuntu has been deprecated since DRAGEN™ v3.9

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Added Functionality

DRAGEN v3.9.5 now supports Red Hat Enterprise Linux (RHEL) v8 for on-site servers. The .run file includes an RPM installer for el8. The installer now uses the Linux dkms service to manage the kernel driver. DRAGEN is tested on Oracle Linux Server release 8.4.

Issues Resolved

Issues that are fixed in v3.9.5

Defect ID	Component	Description
DRAGEN-14274	Cloud Infrastructure	Fix for crash with "HW License V2 expected" on new cloud instance (AWS and Azure) due to a register access attempt before fpga image is loaded.
DRAGEN-14152	All	Fix several security vulnerabilities.
DRAGEN-14188	SNV VC	Fix hang in MNV detection when GVCF mode is enabled.
DRAGEN-14258	Cloud Infrastructure	Fix self_test.sh for AWS instances, allow the license url argument
DRAGEN-14167	SNV VC, Mito	Fix for missing homref scores in Germline Mito GVCF. Somatic homref scores are changed to an evidence measurement rather than a posterior probability, in line with the GQ scores reported for germline homref. This allows zero-depth positions to get a score of zero.
DRAGEN-14380	BCL	Fix a BCL conversion crash when config.xml is present in BaseCalls on aggregated bcl input (HiSeq/MiSeq).
DRAGEN-14297	Somatic CNV	Fix a CNV hang in somatic mode
SET-1971 DRAGEN-14493	SNV VC, Mito	Fix for unexpected MT variant calls with DRAGEN v3.8.4
DRAGEN-13409	BCL	Fix for bcl-convert producing incorrect demuxing data with inputs with a Read 1 size of < 25 cycles
DRAGEN-14430	BCL	BCL fix for AdapterMetrics of R2 being copied from R1
DRAGEN-14080	Downsampling	Fix to propagate full fastq read names to output for downsampling feature
DRAGEN-14179	UMI, HLA	Fix for HLA accuracy degrade when UMI is enabled
DRAGEN-14034 SET-2030	SNV VC	Fix for watchdog timeout (hang) during SNV when haplotypes exceed a certain length
DRAGEN-14460	Downsampling	Fix inconsistent output orientation for Downsampling
DRAGEN-14447	scRNA	Fix out-of-bounds exception in scRNA when using fixed cell threshold
DRAGEN-14501	SNV VC	Block MNV enabling with force GT due to segmentation fault (unsupported)
DRAGEN-14119	scRNA	Fix cell-hashing barcodeSummary.csv output, remove additional empty column
DRAGEN-14495	BCL	Fix BCL convert tiles regex validation error on s_1+s_2

DRAGEN-14538	CRAM	Fix for CRAM index containing invalid span values
DRAGEN-14522	Infrastructure	Add bitstream/fpga tests to self_test.sh
DRAGEN-14479	Cloud Infrastructure	Fix for AMI not working with AWS BATCH / ECS
DRAGEN-14168	SNV VC	Fix a crash during Evidence BAM output when MD tags are enabled
DRAGEN-14040	Somatic CNV	Support T/N+PON CNV WES when running with SNV or SV
DRAGEN-14472	SNV VC, Mito	Fix incorrect callability metric for germline mito GVCF
DRAGEN-13753	SNV VC, Somatic	Fix for forced GT calls present in regions with no coverage and outside of target bed regions in somatic run
DRAGEN-14744	SNV VC, Somatic	Fix for missing NON_REF GVCF positions in Somatic GVCF output
DRAGEN-14781	Gvcf Genotyper, Joint Genotyper	Fix for missing FT fields in ms-VCF header when running Joint Genotyper from Gvcf Genotyper input
DRAGEN-13837	Gvcf Genotyper	Fix for Hail crash on ChrM with Gvcf Genotyper output, by correcting header SQ entry
DRAGEN-14799	Trimmer	Make read-trimming option validation stricter, to resolve potential failure mode
DRAGEN-14798	Trimmer	Add validation check for 'cut-end' trimmer and related trimming options, to resolve potential failure mode

Known Issues

Known issues of the DRAGEN™ v3.9.5 release

Defect ID	Component	Issue Type	Description	Remedy / Workaround
DRAGEN-14966	CRAM, Alt-masking	Bug	CRAM generated with alt-masking HT may not be decodable by 3rd party	Reads which map to regions that are masked may be affected. The workaround is to apply masking to the fasta and use that fasta to decompress the CRAM. The issue is present since alt-masking was introduced in 3.9.3 and will be fixed in DRAGEN v3.10
DRAGEN-14902	Infrastructure	Usability	DRAGEN hangs on corrupted (truncated) BAM input	Some types of BAM truncation may lead to hang in DRAGEN. User will be able to quit the hanging job via CRTL+C and fix their input and re-run.
DRAGEN-14890	SNV VC	Bug	Segmentation fault in MNV	When using the distance bed option to specify combination distances, some bed files lead to a crash in MNV processing. The issue exists in 3.9.3 release. The workaround is to use

				command line option instead of BED file.
DRAGEN-14794	Metrics	Bug	QC region coverage metrics reports more aligned reads than WGS coverage metrics	Use the aligned reads from the WGS coverage metrics
DRAGEN-14755	RNA	Usability	RNA gene fusion output md5sum difference between U200 Phase2 and Phase4 servers due to precision	VCF may not be bit exact match, due to insignificant floating-point differences. The score is used to filter false fusion candidates. Candidates with a score < 0.5 are marked as failing whereas candidates with a score > 0.5 are marked as passing if they also pass other criteria. Based on this, only candidates which have a score close to 0.5 may be affected by this issue, but the issue is seen only on very low score values
DRAGEN-14743	CNV	Usability	Sample excluded from sex genotyper metrics file	A user may include N samples to be used in the panel of normals, for CNV normalization. As part of the algorithm, a sample may be removed from the set if it does not meet certain quality requirements (such as having too many 0 coverage regions). When this happens, the remaining n < N set of samples is used. The remaining n samples will have their Sex Genotype reported in the output cnv_metrics.csv. Known behavior, not a bug. Some users may still be interested in the estimated gender of samples that have been removed, so this will be changed in DRAGEN v3.10
DRAGEN-14727	Metrics, Graph Genome	Bug	DRAGEN graph genome - discrepancy in coverage stats results	A coverage metric for graph genome is incorrect. This issue is present in 3.9.3 also. No workaround
DRAGEN-14526	Methylation	Bug	Multi-pass methylation does not report number of duplicates in mapping metrics.	Duplicates are not reported in metrics for multi-pass methylation. No workaround. The metric is calculated now in the new "single-pass" methylation flow, which is the recommended way to run methylation.
DRAGEN-14513	FPGA	Usability	Deflate engine error: 0x9080 on stream 1 on EAGLE server	Very rare intermittent hardware issue on Phase1 server FPGA leads to crash. Rerun of the sample will succeed.
DRAGEN-14511	Cloud Infrastructure	Usability	[AZURE] Error in `/opt/edico/bin/dragen': corrupted size vs. prev_size: 0x00002b10140015ef	This crash was encountered once on Azure and has not been reproducible. A re-run will succeed
DRAGEN-14390	CRAM	Usability	DRAGEN hits segmentation fault on	When incorrect reference is used to process CRAM input, the system may crash. This has been the behavior of

			CRAM input mismatched with reference	DRAGEN with CRAM input. Select correct reference and re-run.
DRAGEN-14373	Infrastructure	Usability	Trailing whitespace on the dragen command line cause an error	Trailing whitespace can lead to command line parsing error, and dragen exits.
DRAGEN-13977	Infrastructure	Usability	dragen_drv does not compile on linux kernel 5.8.0	dragen driver does not compile on Ubuntu with on linux kernel 5.8.0
DRAGEN-13896	CNV	Bug	Panel of Normals filtering applied incorrectly	Affects CNV panel-of-normals feature, which is still officially supported but no longer recommended. Will not be fixed. The feature shall be deprecated.
DRAGEN-13887	Methylation	Bug	Methylation reporting only assertion failing during processing	Encountered when using methylation report compression. The workaround is to disable report compression
DRAGEN-13818	HT Builder	Usability	Custom reference failing at alignment due to compression issue	Some small custom references cannot be built by the hash table builder. There is no workaround.

SW Installation Procedure

- Download the desired installer from the Illumina support website and unzip the package
- The archive integrity can be checked using: `./<DRAGEN 3.9.3 .run file> --check`
- Install the appropriate release based on your Linux OS with the command: `sudo sh <DRAGEN 3.9.3 .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