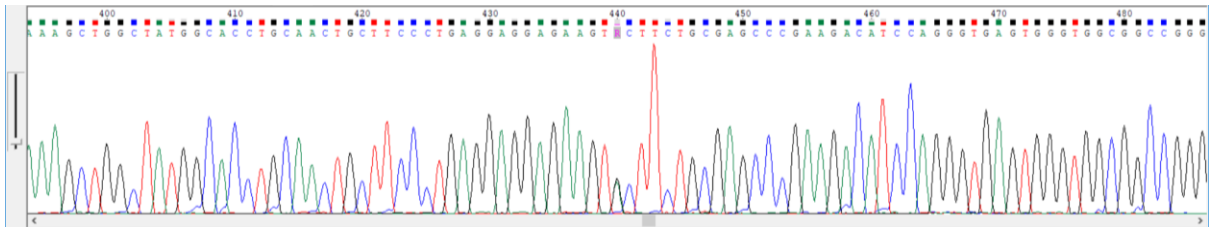
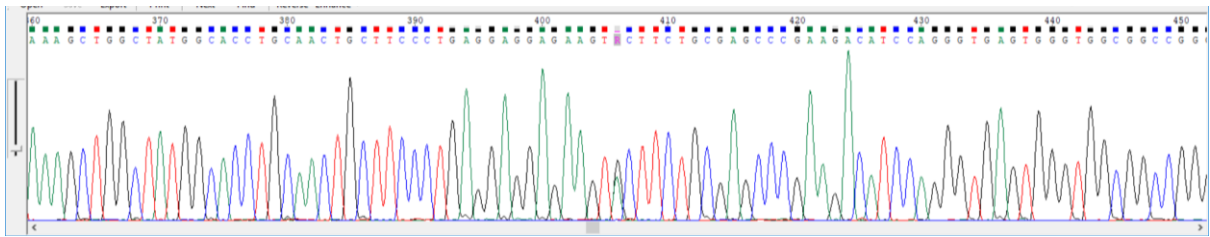


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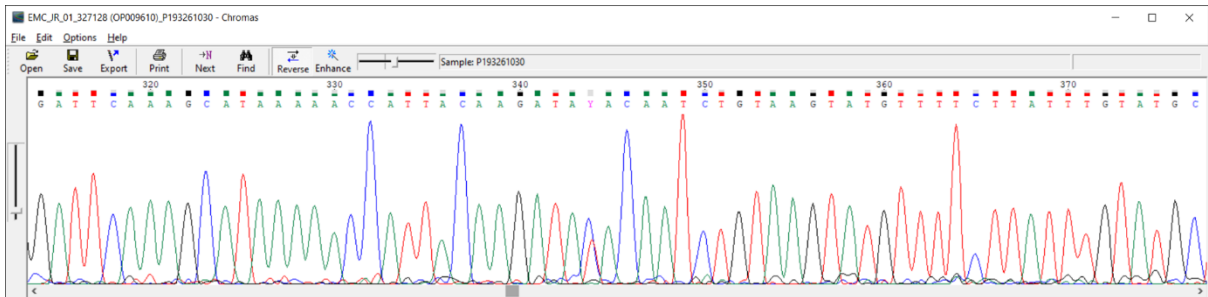
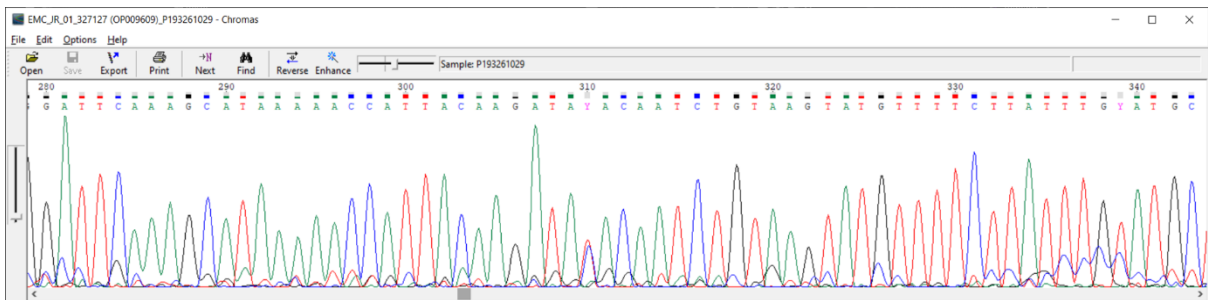
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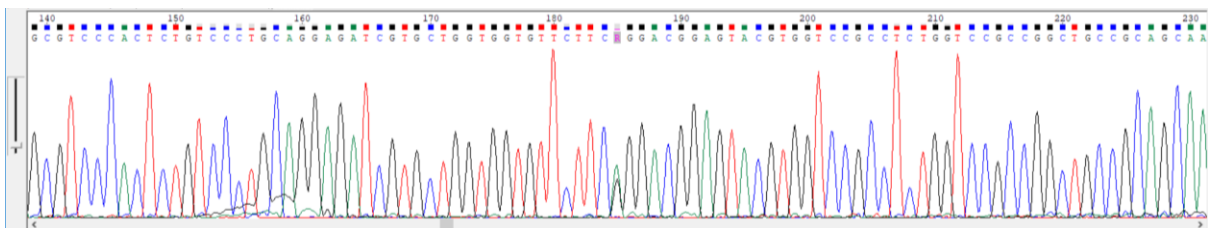
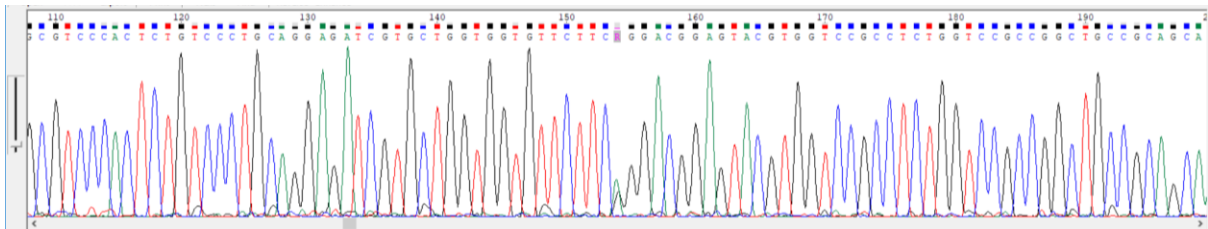
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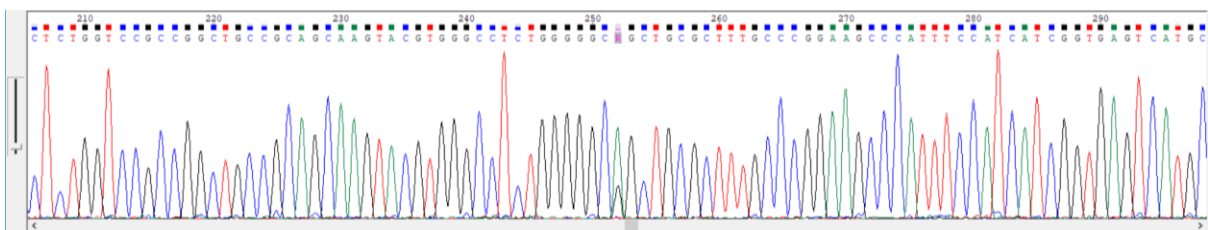
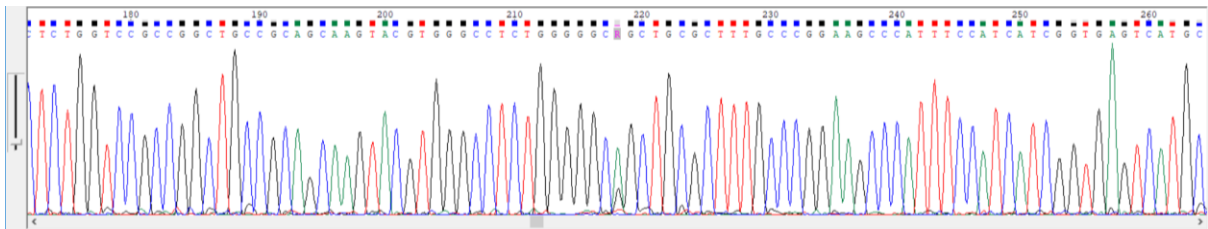
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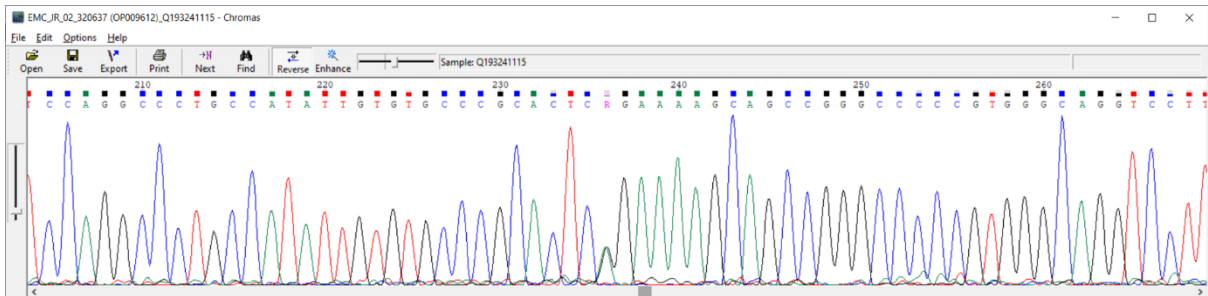
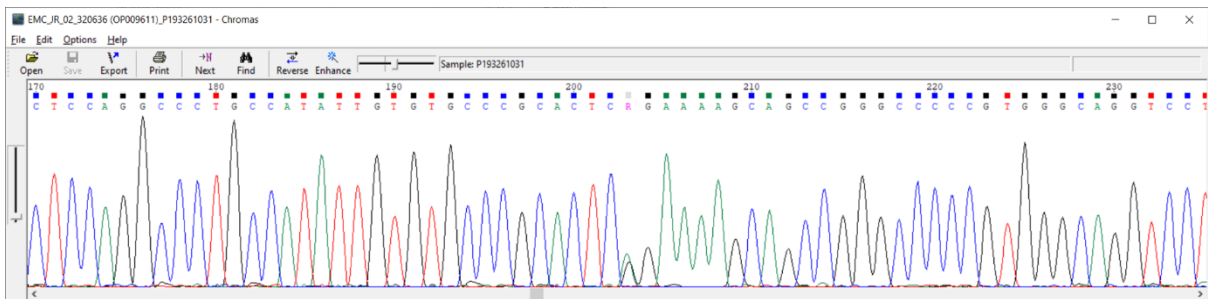
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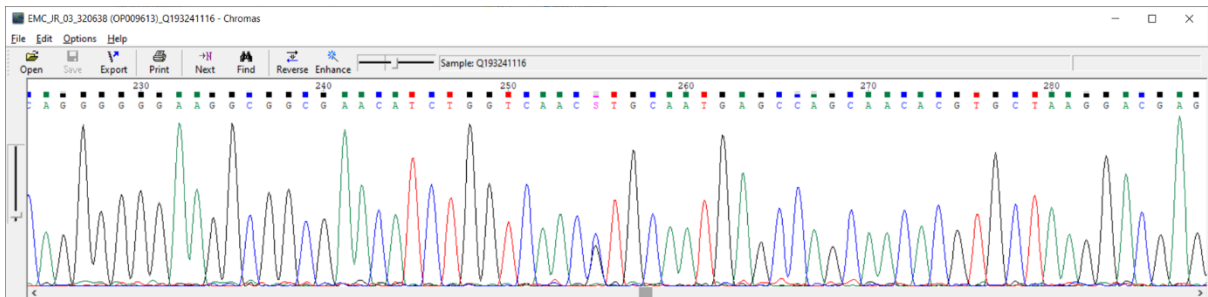
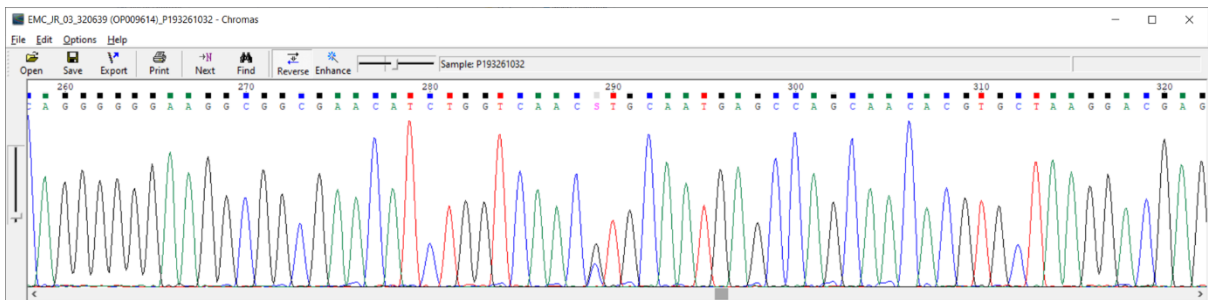
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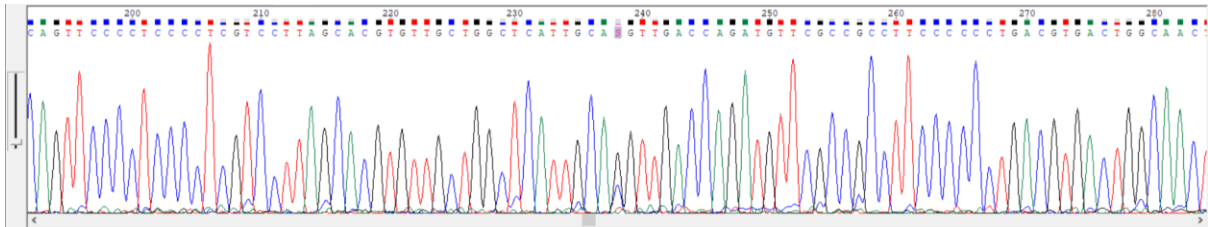
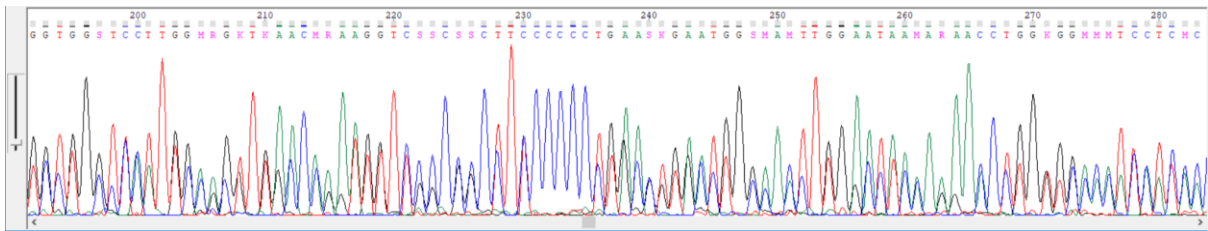
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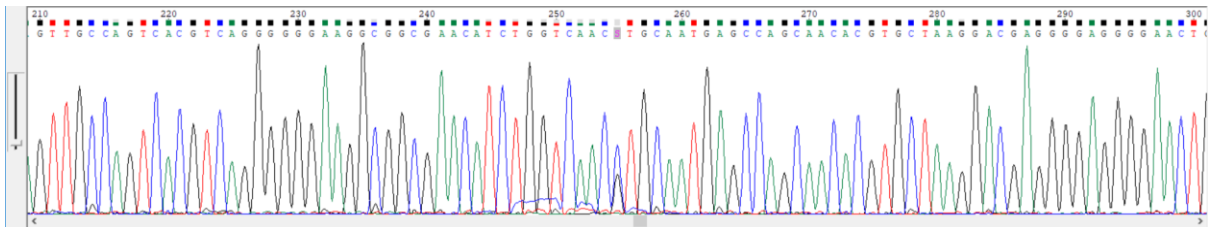
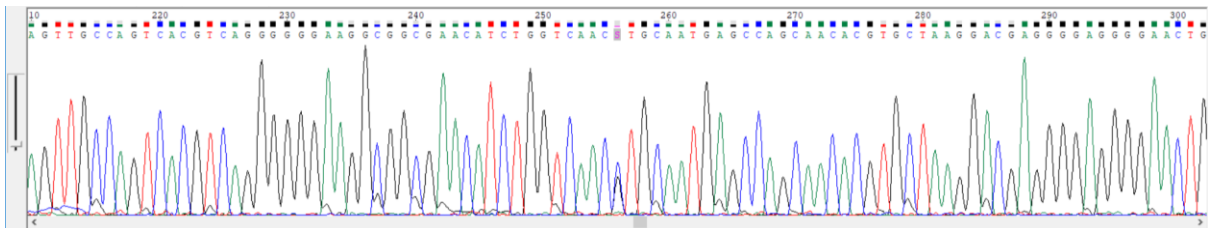
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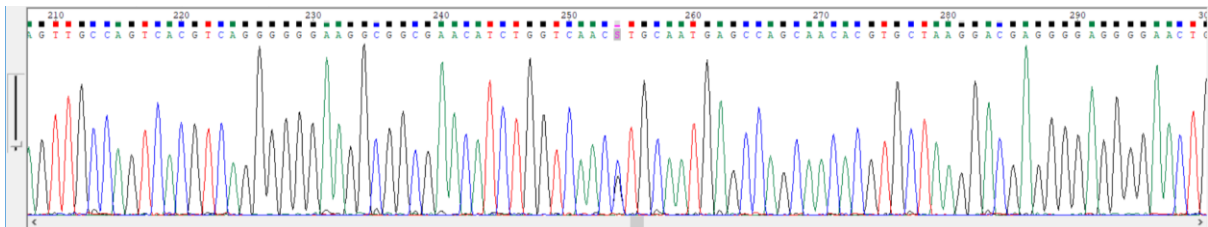
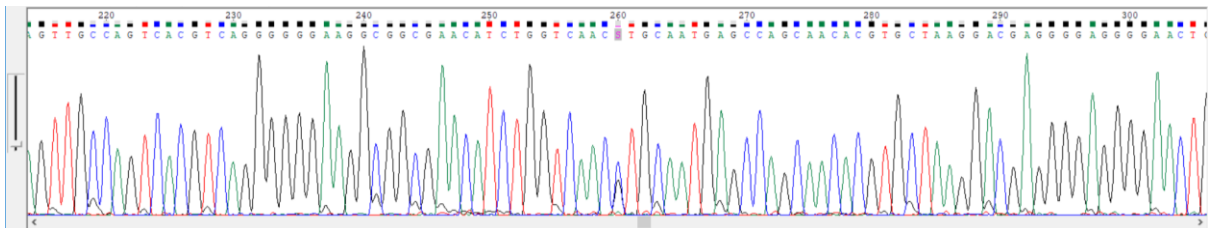
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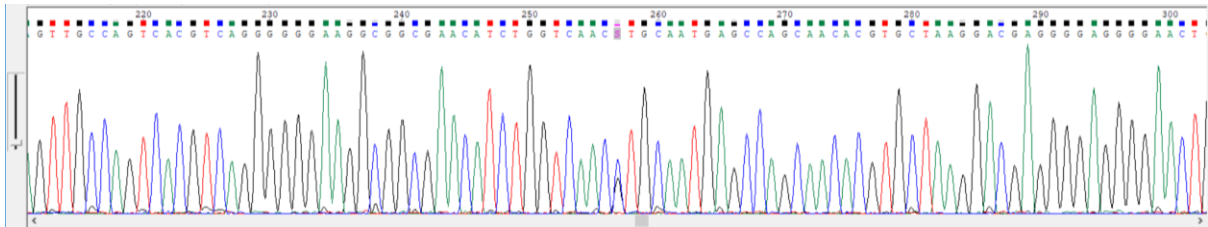
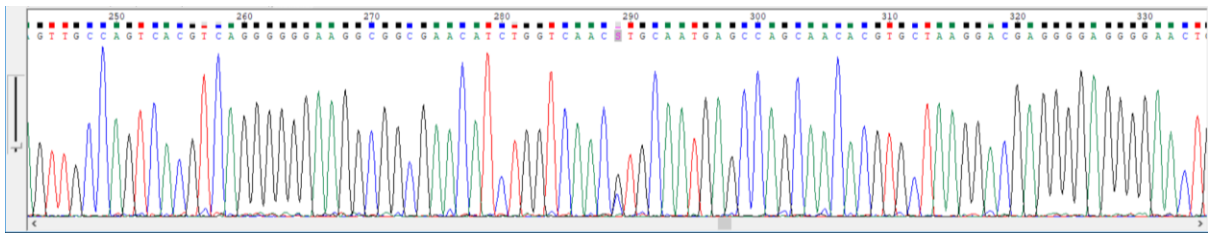
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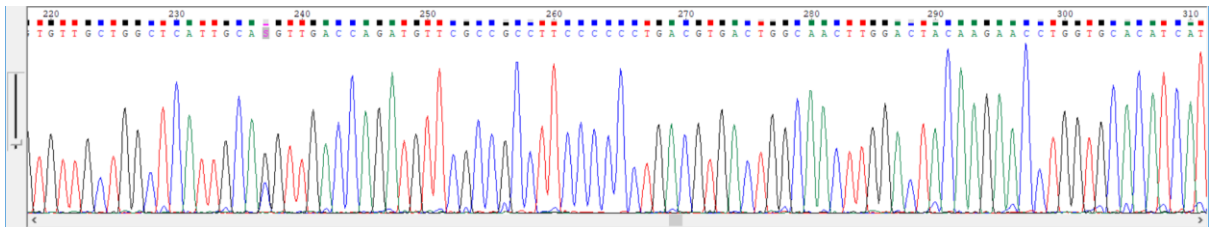
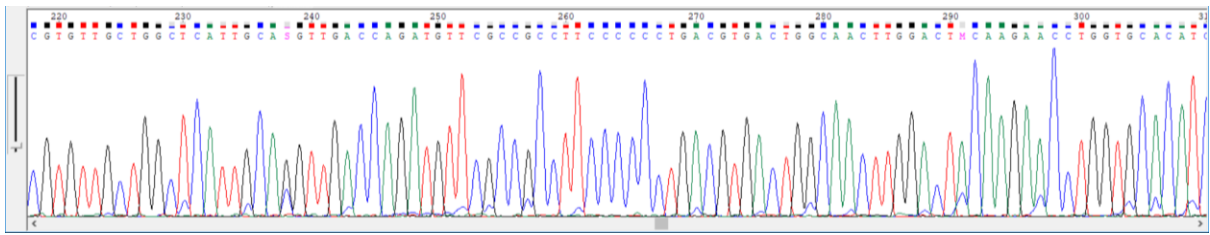
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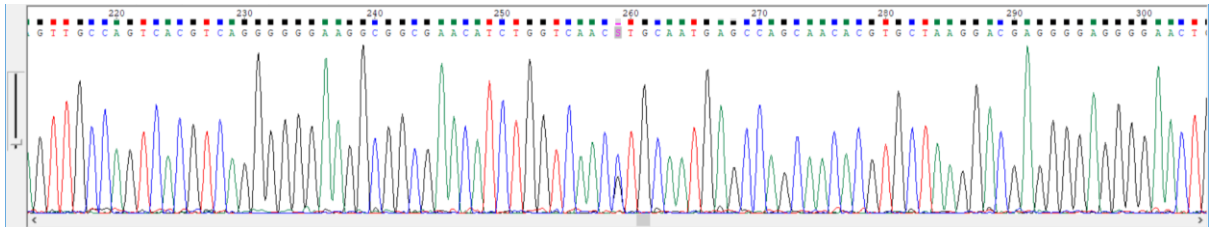
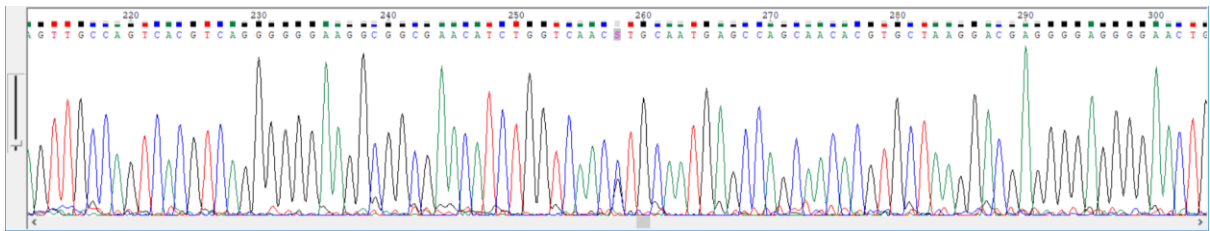
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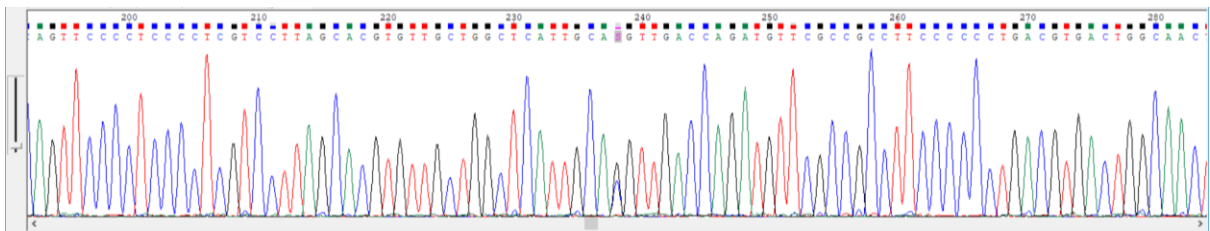
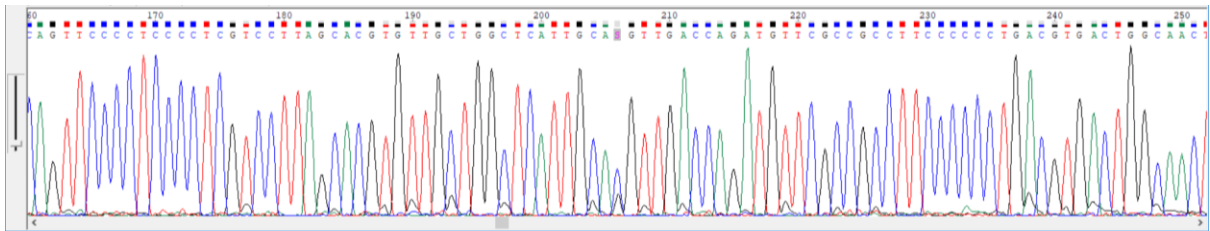
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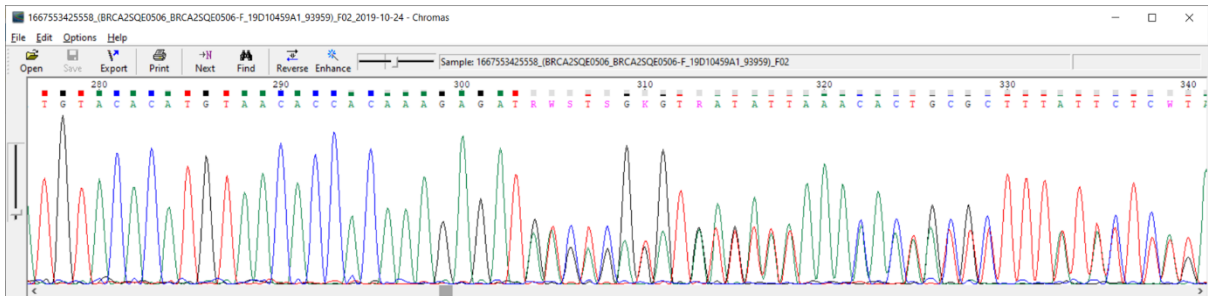
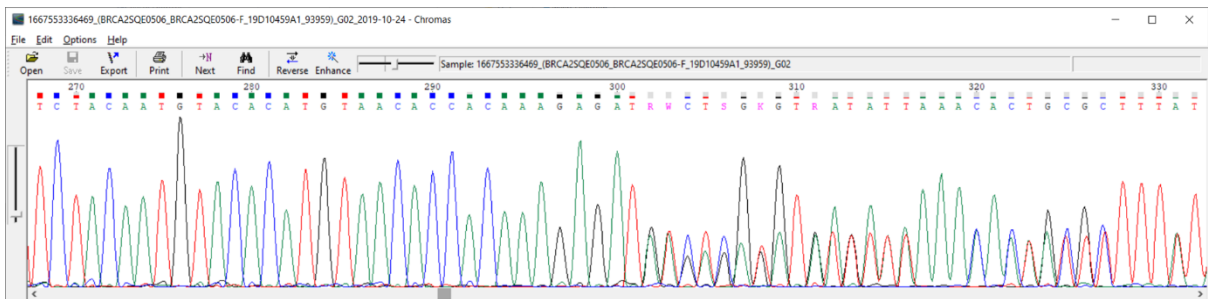
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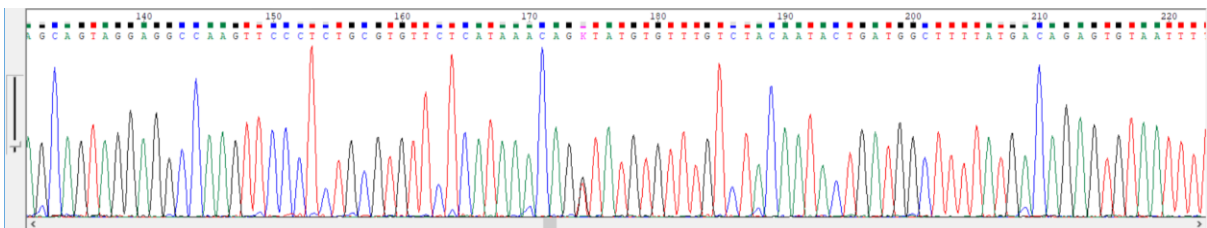
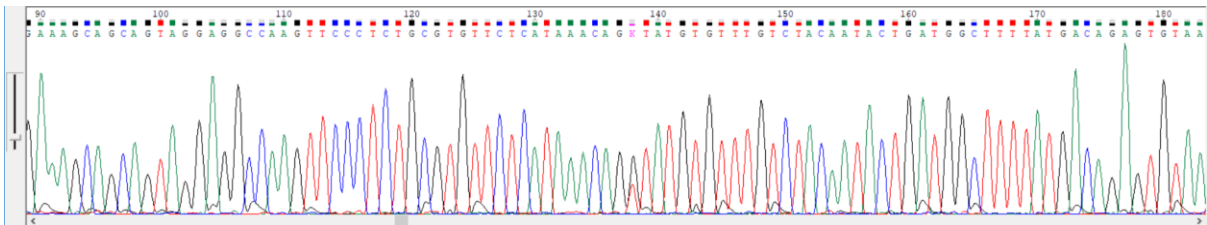
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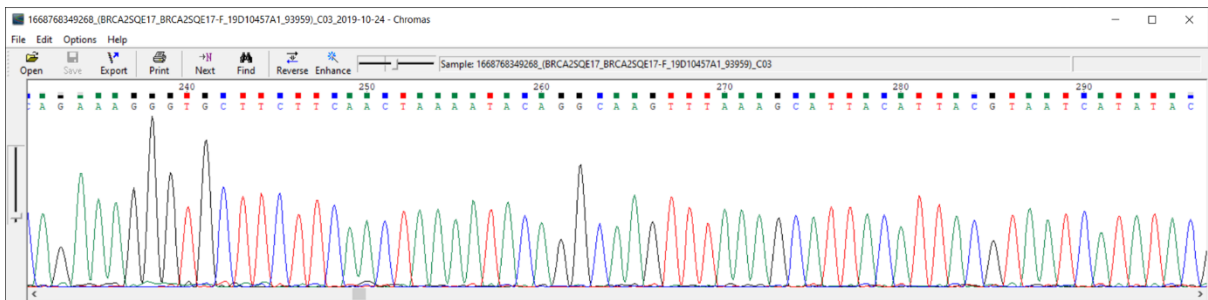
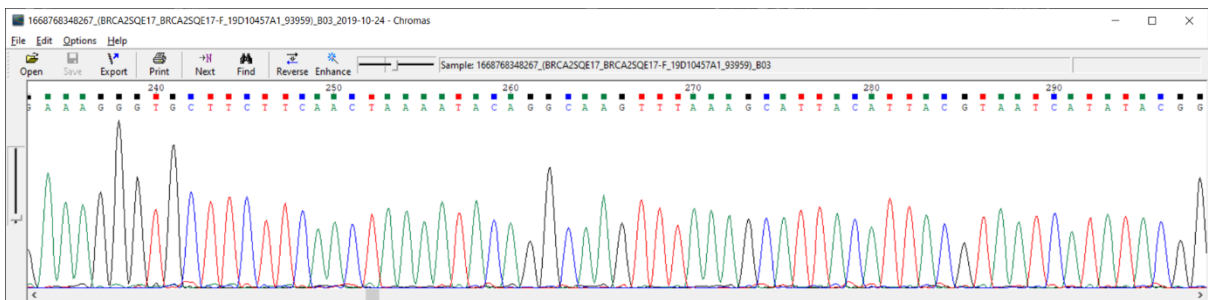
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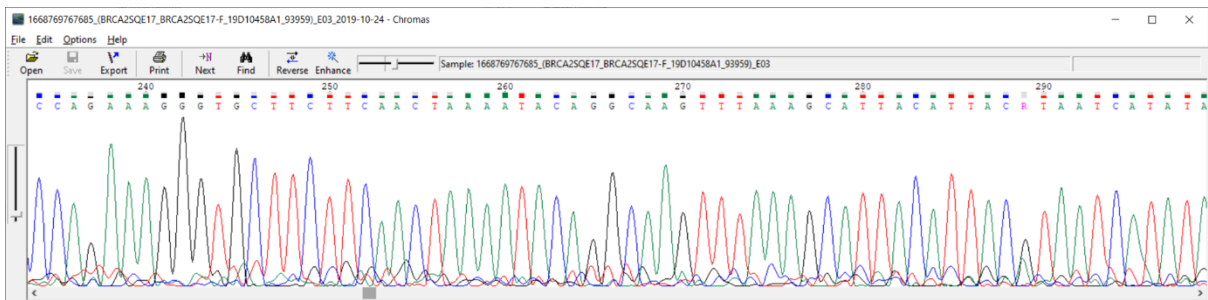
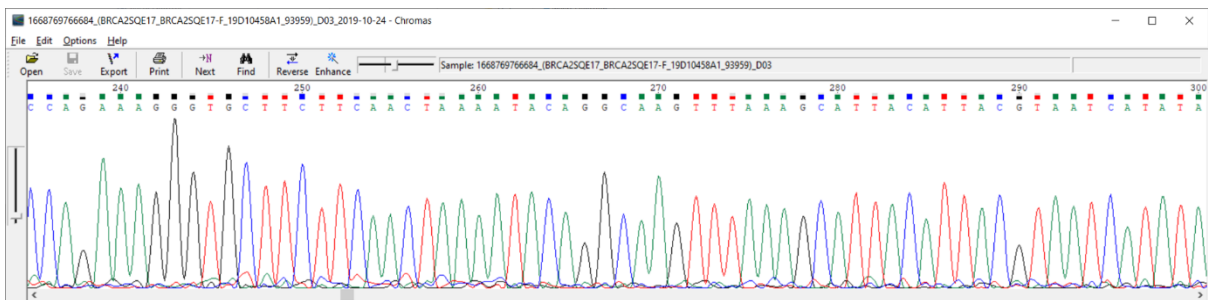
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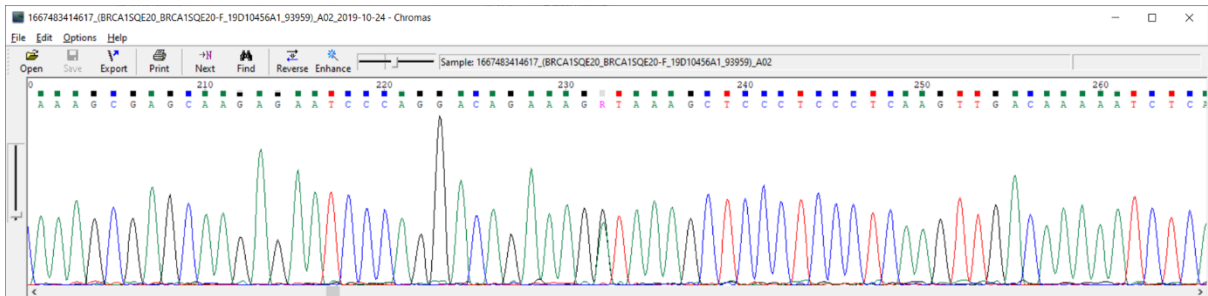
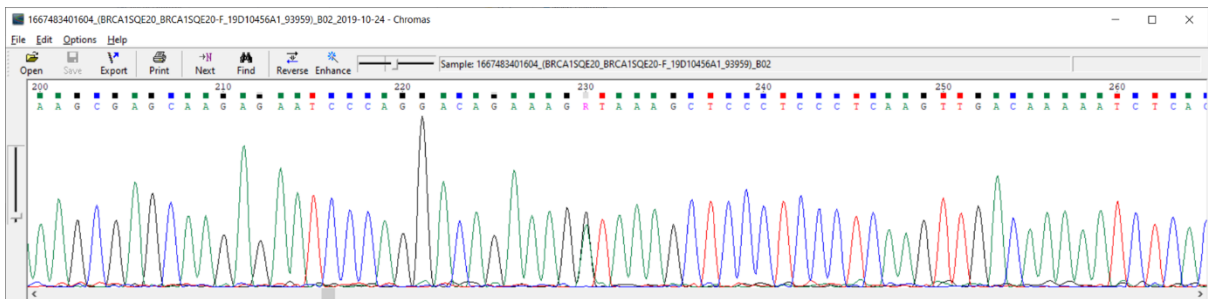
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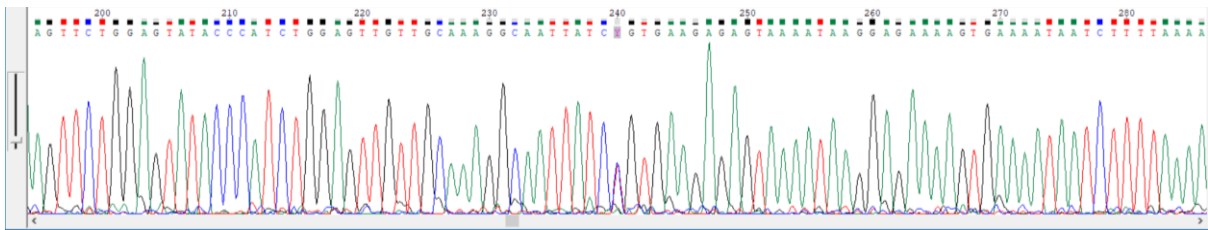
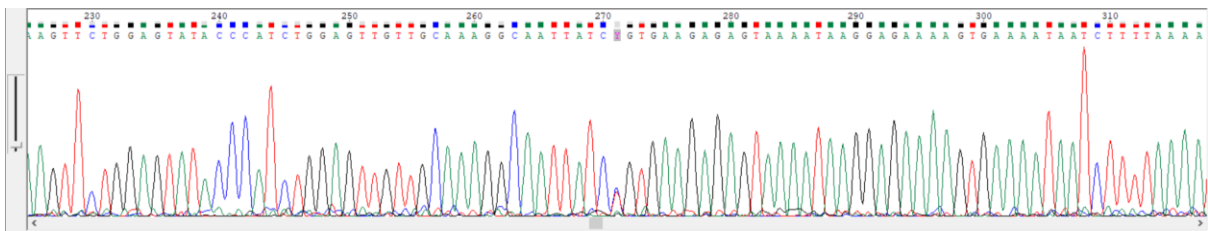
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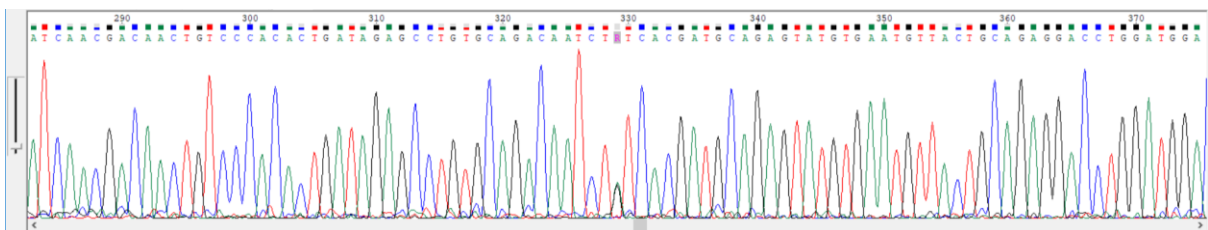
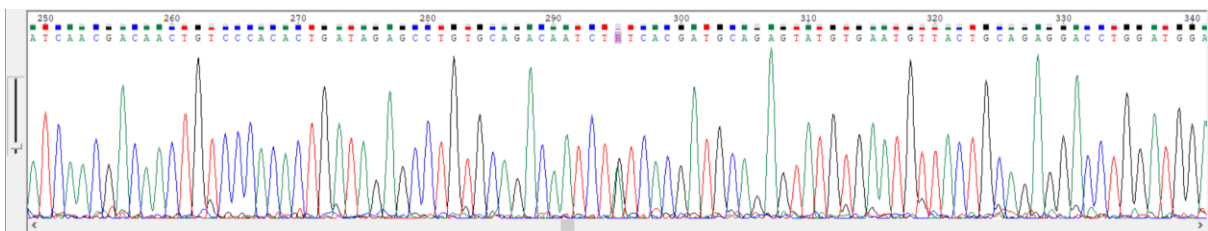
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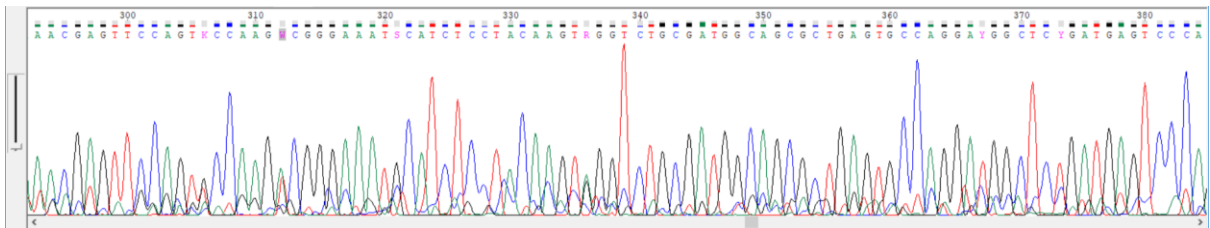
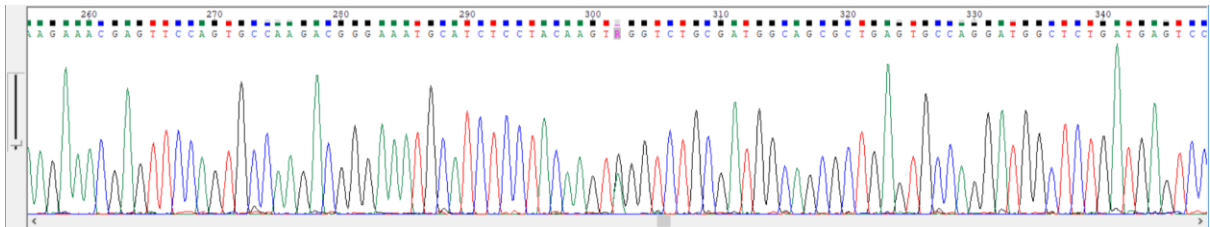
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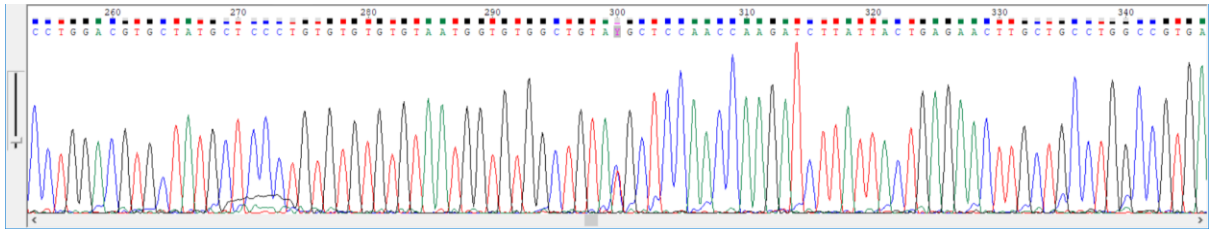
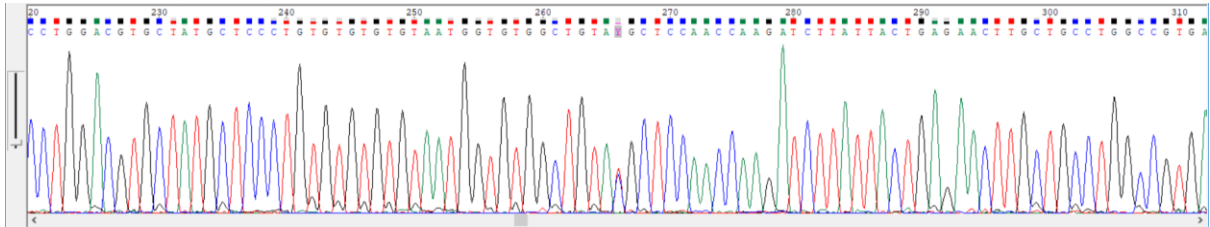
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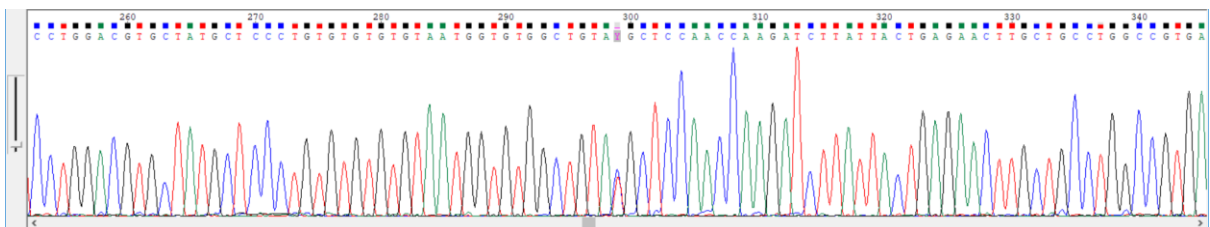
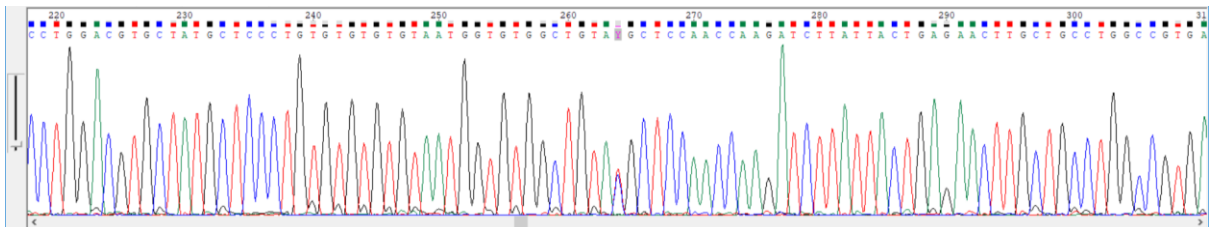
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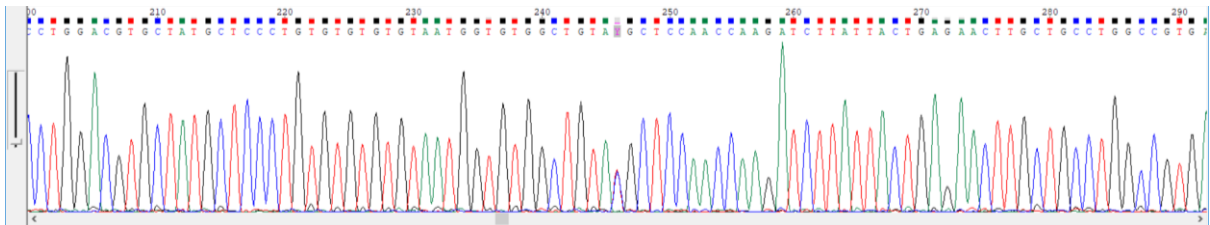
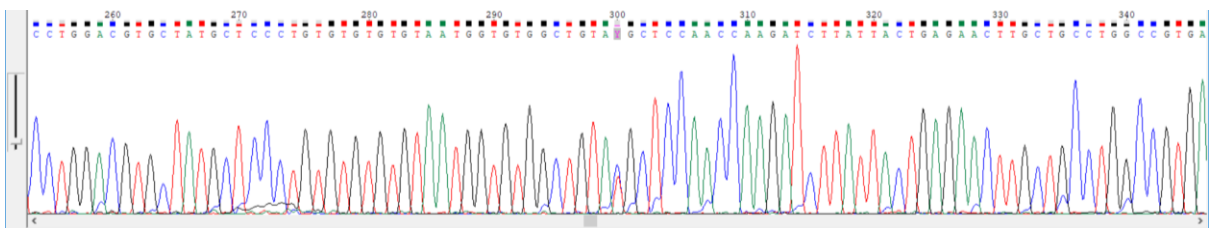
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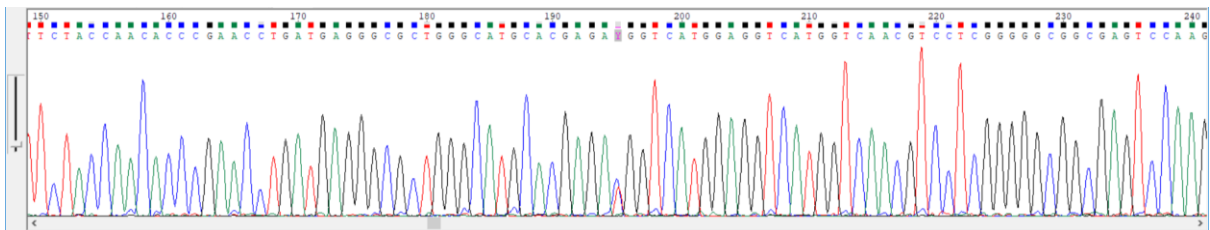
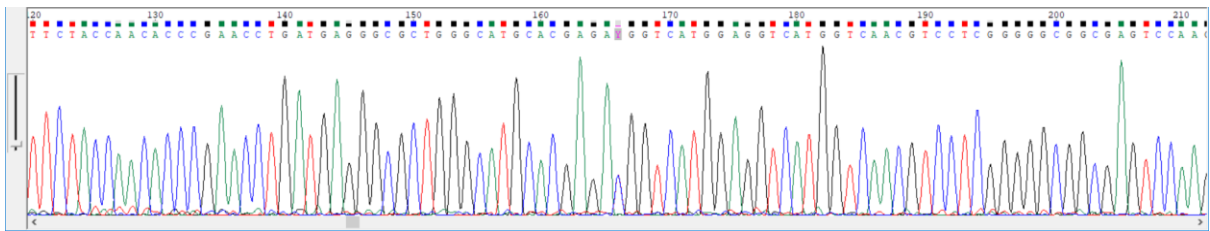
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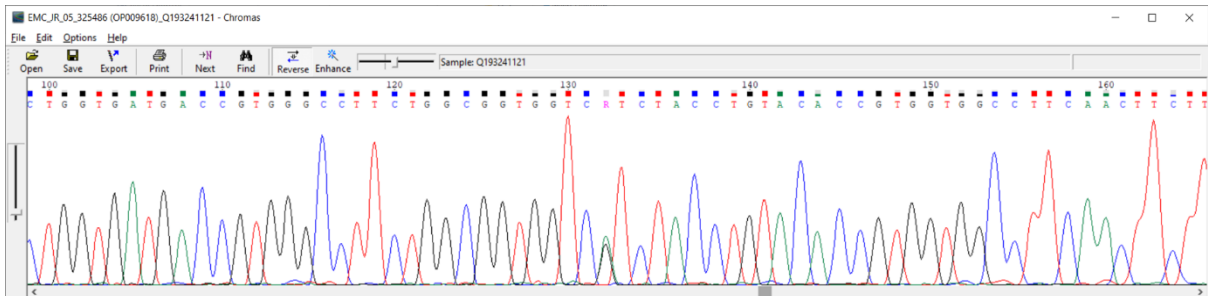
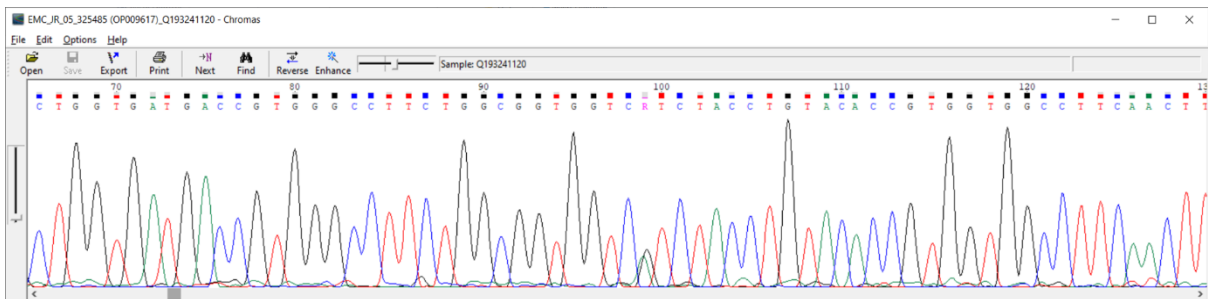
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Supplement 3; Event Z-scores of three KP variant carriers

Carrier	ICD10	Description	Age at Event	Total Number of Events	Average Event Age (SD)	Z-score
D1	I48	Atrial Fibrillation	64	547	77 (10)	-1.3
D1	I46	Cardiac arrest	81	121	81 (8)	0.0
F4	I21	Myocardial Infarction	72	354	79 (8)	-0.9
F4	I21	Myocardial Infarction	72	354	79 (8)	-0.9
F4	I21	Myocardial Infarction	73	354	79 (8)	-0.8
F4	I21	Myocardial Infarction	77	354	79 (8)	-0.3
F4	R99	Death, cause unknown	85	165	87 (7)	-0.3
F7	I20	Angina Pectoris	69	141	72 (8)	-0.4
F7	I50	Heart Failure	69	760	80 (8)	-1.4

Supplement 4; Methods of phenotype collection

Supplementary methods; collection of ICD10 based phenotypic events

Follow-up started after the baseline home interview of each individual participant. Data on clinical outcomes of interest are collected continuously through an automated follow-up system. The follow-up system involves automated digital linkage of the study database to digital files from general practitioners (GPs) in the study area. On a weekly basis, all ICPC codes of relevant diagnoses made by the GPs and medical specialists in study participants are entered to the Rotterdam Study database.

Moreover, the entire medical record of each participant living in the research area is checked manually on a regular basis at the GPs' office by trained research assistants for diagnoses of interest. This is the primary source of information on incident events, since all letters of medical specialists, discharge reports in case of hospitalization, and additional information are copied by the research assistants. Additional information is obtained from the hospitals in case the automated follow-up system or medical records contain insufficient information.

Medical records of the participants under the care of nursing home physicians or GPs working outside the study area are checked annually for potential events (this holds for approximately 15% of all participants).

Subsequently, all the collected information is compared to the ICPC codes already entered to the study database for each individual participant. This is done in order to make sure no clinical information on potential events is missed out. Furthermore, before every repeat examination at the research center the participants are interviewed on the occurrence of new events since their last visit.

With respect to the vital status of all participants, information is obtained on a weekly basis from the central registry of the municipality in Rotterdam and through the digital linkage with GPs working in the study area. For participants living outside the research area, the GPs are the primary source of information, complemented by the municipality records in the place of residence. After notification, cause and circumstances of death are established by requesting information from the medical records of the GPs or nursing home physicians.