

Ontologies Classes Object Properties Data Properties Annotation Properties Individuals Datatypes Clouds

Class: Smokers_SCLC

Annotations (2)

- rdfs:comment** "Overall, we describe an improved DELFI approach for genome-wide fragmentation analyses for the detection of lung cancer. We propose that facile and scalable analyses of cfDNA fragmentomes could be used to prescreen high-risk populations for lung cancer to increase the accessibility of lung cancer detection and decrease unnecessary follow-up imaging procedures and invasive biopsies. Through the analysis of the LUCAS cohort, we demonstrated that the DELFI approach can detect lung cancer across all stages and histologic subtypes compared to non-cancer individuals with or without benign lung nodules. The validation of the fixed DELFI model from the LUCAS cohort in an independent validation cohort supports the generalizability of the approach. Similar to observations with targeted sequencing approaches^{16,22,39,40,41,42,43}, the relationship between DELFI scores and tumor progression and long-term mortality suggests that the blood-based fragmentation analyses may identify occult disease not observed by imaging, or more accurately identify the aggressiveness of the disease. The distinction between NSCLC and SCLC may allow for non-invasive characterization and treatment of lung cancer patients when tissues are not available. The identification of patients by DELFI that were only found months later to have cancer through standard diagnostic methods shows the utility of the approach for cancer detection, detection of recurrent disease, and the potential for detection of cancers at earlier stages ("stage shifting") through lung cancer screening. The possibility of combining genome-wide multi-feature fragmentation profile analyses with a standard protein marker and clinical characteristics provides an avenue for high complexity multimodal analyses that can further increase the sensitivity of the approach."
- rdfs:comment** "We examined patient blood samples from a prospective observational trial of 365 individuals examined consecutively at Bispebjerg Hospital in Copenhagen, Denmark (LUCAS cohort) during a seven-month period. The majority of subjects in the cohort were symptomatic individuals at high risk for lung cancer (age 50–80 and smoking history >20 pack-years) (Table 1, Supplementary Table 1). The cohort included 323 subjects (90%) with pulmonary, non-pulmonary or constitutional symptoms, with the majority having common smoking-related symptoms such as cough or dyspnea. The remainder were asymptomatic at enrollment, with an incidental chest image finding by X-ray or CT that was suspicious for lung malignancy. At the time of the patient's clinic visit, an additional chest CT or 18F-PET/CT was performed to assess the identified nodule or infiltrate (Supplementary Fig. 1). Of the 365 individuals studied, 129 were determined to have lung cancer a few days after the time of the blood collection (median 9.5 days, range 0–44) while the remainder had histologically proven benign nodules (n = 87) or were not biopsied due to low clinical and radiographic suspicion for cancer (n = 149) (Supplementary Fig. 1). Standard algorithms for the management of pulmonary nodules, including the Fleischner Society pulmonary nodule recommendations^{24,25,26}, were used to determine clinical management. Table 1 Patient demographics and clinical information in LUCAS cohort. Full size table We isolated 2–4 ml of plasma from each patient in the LUCAS cohort and examined the extracted cfDNA using the DELFI approach with experimental and bioinformatic improvements. As PCR is known to affect the representation of amplified genomic fragments depending on GC content and fragment length, we evaluated DELFI genome-wide fragmentation profiles using genomic libraries created without amplification or with 4 or 12 cycles of PCR. We found that libraries created with 4 cycles of PCR had profiles that were similar to those without any amplification, while 12 cycles led to substantial biases (Supplementary Fig. 2a, b). We developed a novel fragment-based GC correction method that simultaneously accounts for preferential amplification by fragment length and/or GC content (see "Methods"). We examined whether this approach among 4 cycle libraries would further minimize GC biases compared to a commonly used bin-based approach²⁷ and found that the fragment-based approach was closest to the libraries without amplification (Supplementary Fig. 2c). We therefore used a 4 cycle amplification to generate genomic libraries, and sequenced the genomic fragments using shallow whole-genome sequencing (~2x coverage) with an average of 40 million paired reads per sample (Fig. 1, Supplementary Table 2). To examine genome-wide cfDNA fragmentation patterns, we used the fragment-based GC corrected sequence data to evaluate fragmentation profiles across the genome in 473 non-overlapping 5 MB regions with high mappability, each region comprising ~80,000 fragments, and spanning approximately 2.4 GB of the genome. The resulting fragmentation profiles were remarkably consistent among non-cancer individuals, including those with non-malignant lung nodules (Fig. 2a, b). In contrast, cancer patients displayed widespread genome-wide variation (Fig. 2a, b). Remarkably, the fragmentation profile differences could be observed in multiple regions throughout the genome for the majority of cancer patients, including across stages and histologies. We employed a machine learning model to examine whether cfDNA profiles had characteristics of an individual with or without lung cancer. Due to the high dimensionality of our genome-wide fragmentation profiles relative to the number of patients analyzed, we performed a principal component analysis (PCA) to identify linear combinations of our fragmentation features that explained at least 90% of the variance. We incorporated this dimensionality reduction step into a machine learning model and estimated the performance characteristics by repeated fivefold cross-validation, generating a score for each individual as an

average over the cross-validation repeats (DELFI score). Analysis of the features incorporated in the machine learning models and corresponding measures of variable importance revealed fragmentation and chromosomal changes that were altered in cancer patients and predictive of cancer risk (Fig. 2c). The importance of these features were consistent across the training folds (Supplementary Fig. 3). Among the genomic changes incorporated in the model, chromosomal arms that were increased or decreased in cfDNA representation corresponded to those commonly gained or lost in lung cancer as seen in previous TCGA large-scale genomic studies for lung adenocarcinoma (n = 518) and squamous cell carcinoma (n = 501) (Fig. 2c). These included increased cfDNA levels of 7q, 12p, and 20q, or decreased levels of 1p, 3p, 8p, and 17p, all known to be gained or lost, respectively, in a variety of lung cancers^{28,29,30}."

Superclasses (1)

- Small_Cell_Lung_Cancer

Disjoints (690)

'\Abraxane_(Paclitaxel_Albumin-stabilized_Nanoparticle_Formulation)_\'', '\Afinitor_(Everolimus)_\'', '\Afinitor_Disperz_(Everolimus)_\'', '\Alecensa_(Alectinib)_\'', '\Alimta_(Pemetrexed_Disodium)_\'', '\Alunbrig_(Brigatinib)_\'', '\Alymsys_(Bevacizumab)_\'', '\Avastin_(Bevacizumab)_\'', '\Cyramza_(Ramucirumab)_\'', '\Enhertu_(Fam-Trastuzumab_Deruxtecan-nxki)_\'', '\Etopophos_(Etoposide_Phosphate)_\'', '\Exkivity_(Mobocertinib_Succinate)_\'', '\Gavreto_(Pralsetinib)_\'', '\Gemzar_(Gemcitabine_Hydrochloride)_\'', '\Gilotrif_(Afatinib_Dimaleate)_\'', '\Hycamtin_(Topotecan_Hydrochloride)_\'', '\Imfinzi_(Durvalumab)_\'', '\Imjudo_(Tremelimumab-actl)_\'', '\Infugem_(Gemcitabine_Hydrochloride)_\'', '\Iressa_(Gefitinib)_\'', '\Keytruda_(Pembrolizumab)_\'', '\Krazati_(Adagrasib)_\'', '\Libtayo_(Cemiplimab-rwlc)_\'', '\Lorbrena_(Lorlatinib)_\'', '\Lumakras_(Sotorasib)_\'', '\Mekinist_(Trametinib_Dimethyl_Sulfoxide)_\'', '\Mvasi_(Bevacizumab)_\'', '\Opdivo_(Nivolumab)_\'', '\Portrazza_(Necitumumab)_\'', '\Retevmo_(Selpercatinib)_\'', '\Rozlytrek_(Entrectinib)_\'', '\Rybrevant_(Amivantamab-vmjw)_\'', '\Tabrecta_(Capmatinib_Hydrochloride)_\'', '\Tafinlar_(Dabrafenib_Mesylate)_\'', '\Tagrisso_(Osimertinib_Mesylate)_\'', '\Taxotere_(Docetaxel)_\'', '\Tecentriq_(Atezolizumab)_\'', '\Tepmetko_(Tepotinib_Hydrochloride)_\'', '\Trexall_(Methotrexate_Sodium)_\'', '\Vizimpro_(Dacomitinib)_\'', '\Xalkori_(Crizotinib)_\'', '\Yervoy_(Ipilimumab)_\'', '\Zirabev_(Bevacizumab)_\'', '\Zykadia_(Ceritinib)_\'', 4A_NSCLC, 4B_NSCLC, Adagrasib_, Adherence_Based_on_Socioeconomics_LC, Adherence_Factors_LC, Adverse_Reactions_ABAX, Adverse_Reactions_ADAGR, Adverse_Reactions_AFATI, Adverse_Reactions_AFINI, Adverse_Reactions_AFINIT, Adverse_Reactions_ALECE, Adverse_Reactions_ALIMT, Adverse_Reactions_ALUNB, Adverse_Reactions_ARYMS, Adverse_Reactions_AMIVA, Adverse_Reactions_ATEZO, Adverse_Reactions_AVAST, Adverse_Reactions_BRIGA, Adverse_Reactions_CAPMA, Adverse_Reactions_CEMIP, Adverse_Reactions_CYRAM, Adverse_Reactions_DOXOR, Adverse_Reactions_DURVA, Adverse_Reactions_ENHER, Adverse_Reactions_ENTRE, Adverse_Reactions_ERLOT, Adverse_Reactions_ETOP, Adverse_Reactions_ETOPO, Adverse_Reactions_EXKIV, Adverse_Reactions_GAVRE, Adverse_Reactions_GEFIT, Adverse_Reactions_GEMZA, Adverse_Reactions_GILOT, Adverse_Reactions_HYCAM, Adverse_Reactions_IMFIN, Adverse_Reactions_IMJUD, Adverse_Reactions_INFUG, Adverse_Reactions_IRESS, Adverse_Reactions_KEYTR, Adverse_Reactions_KRAZA, Adverse_Reactions_LIBTA, Adverse_Reactions_LORBR, Adverse_Reactions_LUMAK, Adverse_Reactions_LURB, Adverse_Reactions_MEKIN, Adverse_Reactions_METH, Adverse_Reactions_MVASI, Adverse_Reactions_OPDIV, Adverse_Reactions_PORTR, Adverse_Reactions_RAMUC, Adverse_Reactions_RETEV, Adverse_Reactions_ROZLY, Adverse_Reactions_RYBRE, Adverse_Reactions_SELPE, Adverse_Reactions_SOTOR, Adverse_Reactions_TABRE, Adverse_Reactions_TAFIN, Adverse_Reactions_TAGRIS, Adverse_Reactions_TAXOT, Adverse_Reactions_TECEN, Adverse_Reactions_TEPME, Adverse_Reactions_TOPO, Adverse_Reactions_TRAME, Adverse_Reactions_TREME, Adverse_Reactions_TREXA, Adverse_Reactions_VINOR, Adverse_Reactions_VIZIM, Adverse_Reactions_XALKO, Adverse_Reactions_YERVO, Adverse_Reactions_ZIRAB, Adverse_Reactions_ZYKAD, Afatinib_Dimaleate_, Age, Air_Pollution, Amivantamab-vmjw_, Atezolizumab_, Behavioral_Factors_LC, Beta_Carotene_Supplements_LC, Bio_Sensors_LC, Biological_Effects_LC, Breathalyzer_LC, Breathing_LC, Brigatinib_, Capmatinib_Hydrochloride_, Causes_and_Risks_LC, Cemiplimab-rwlc_, Chemical_Sensors_LC, Choosing_Quality_of_Life_-_Reasons_People_Forego_Treatment, Choosing_Survival_-_Deciding_to_Undergo_Treatment, Complications_LC, Contraindications_ABAX, Contraindications_ADAGR, Contraindications_AFATI, Contraindications_AFINI, Contraindications_AFINIT, Contraindications_ALECE, Contraindications_ALIMT, Contraindications_ALUNB, Contraindications_ARYMS, Contraindications_AMIVA, Contraindications_ATEZO, Contraindications_AVAST, Contraindications_BRIGA, Contraindications_CAPMA, Contraindications_CEMIP, Contraindications_CYRAM, Contraindications_DOXOR, Contraindications_DURVA, Contraindications_ENHER, Contraindications_ENTRE, Contraindications_ERLOT, Contraindications_ETOP, Contraindications_ETOPO, Contraindications_EXKIV, Contraindications_GAVRE, Contraindications_GEFIT, Contraindications_GEMZA, Contraindications_GILOT, Contraindications_HYCAM, Contraindications_IMFIN, Contraindications_IMJUD, Contraindications_INFUG, Contraindications_IRESS, Contraindications_KEYTR,

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 Cultural_Beliefs_and_Perceptions, Cultural_LC, Degrees_of_Smoking_LC, Demographic_Factors_LC, Diet_LC,
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 Dosage_Forms_and_Strengths_YERVO, Dosage_Forms_and_Strengths_ZIRAB,
 Dosage_Forms_and_Strengths_ZYKAD, Doxorubicin_Hydrochloride_, Drug_Interactions_ABRAX,

Drug_Interactions_ADAGR, Drug_Interactions_AFATI, Drug_Interactions_AFINI, Drug_Interactions_AFINIT, Drug_Interactions_ALECE, Drug_Interactions_ALIMT, Drug_Interactions_ALUNB, Drug_Interactions_ALYMS, Drug_Interactions_AMIVA, Drug_Interactions_ATEZO, Drug_Interactions_AVAST, Drug_Interactions_BRIGA, Drug_Interactions_CAPMA, Drug_Interactions_CEMIP, Drug_Interactions_CYRAM, Drug_Interactions_DOXOR, Drug_Interactions_DURVA, Drug_Interactions_ENHER, Drug_Interactions_ENTRE, Drug_Interactions_ERLOT, Drug_Interactions_ETOP, Drug_Interactions_ETOPO, Drug_Interactions_EXKIV, Drug_Interactions_GAVRE, Drug_Interactions_GEFIT, Drug_Interactions_GEMZA, Drug_Interactions_GILOT, Drug_Interactions_HYCAM, Drug_Interactions_IMFIN, Drug_Interactions_IMJUD, Drug_Interactions_INFUG, Drug_Interactions_IRESS, Drug_Interactions_KEYTR, Drug_Interactions_KRAZA, Drug_Interactions_LIBTA, Drug_Interactions_LORBR, Drug_Interactions_LUMAK, Drug_Interactions_LURB, Drug_Interactions_MEKIN, Drug_Interactions_METH, 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Marijuna_Smoking_LC, Medications_LC, Methotrexate_Sodium_, Never-Smokers_LC, Non-Small_Cell_LC, Non-Small_Cell_LC_NSCLC, Non-Small_Cell_Lung_Cancer, Non-Small_Cell_Medication_LC_, Non-Smokers_LC, Non-Smokers_NSCLC, Non-Smokers_SCLC, Nutrition_LC, Occupational_Exposure, Physical_Activity_For_Mitigation_of_LC, Physical_Activity_For_Prevention_Of_LC, Preventative_habits_LC, Quitting/Not_Smoking_LC, Racial/Ethnic, Radiation_Exposure_LC, Ramucirumab_, Recurring_LC_NSCLC, Recurring_LC_SCLC, Rural_LC, Second-hand_Smoke_LC, Secondhand_Smoke_LC, Selpercatinib_, Sensor_Factors_LC, Size_of_the_community_LC, Sleep_LC, Small_Cell_LC, Small_Cell_LC_SCLC, Small_Cell_Medication_LC_, Smoke_LC, Smokers_LC, Smokers_NSCLC, **Smokers_SCLC**, Smoking_LC, Smoking_Marijuana_LC, Smoking_Other_Drugs_LC, Smoking_Tobacco_LC, Socioeconomics_LC, Sotorasib_, Stage_0_NSCLC, Stage_1_NSCLC, Stage_1_SCLC, Stage_2_NSCLC, Stage_3A_NSCLC, Stage_3B_NSCLC, Stage_4_NSCLC, Support_Groups_LC, Symptoms_and_Tests_LC, Symptoms_NSC, Symptoms_SC, Tests_NSC, Tests_SC, Tobacco_Smoking, Tobacco_Smoking_LC, Topotecan_Hydrochloride_, Tramentinib_Dimethyl_Sulfoxide, Treatment_Regimens_LC, Treatments_LC, Tremelimumab-actl_, Urban_LC, Use_in_Specific_Populations_ABRAX, Use_in_Specific_Populations_ADAGR, Use_in_Specific_Populations_AFATI, Use_in_Specific_Populations_AFINI, Use_in_Specific_Populations_AFINIT, Use_in_Specific_Populations_ALECE, Use_in_Specific_Populations_ALIMT, Use_in_Specific_Populations_ALUNB, Use_in_Specific_Populations_ALYMS, Use_in_Specific_Populations_AMIVA, Use_in_Specific_Populations_ATEZO, Use_in_Specific_Populations_AVAST, Use_in_Specific_Populations_BRIGA, Use_in_Specific_Populations_CAPMA, Use_in_Specific_Populations_CEMIP, Use_in_Specific_Populations_CYRAM, Use_in_Specific_Populations_DOXOR, Use_in_Specific_Populations_DURVA, Use_in_Specific_Populations_ENHER, Use_in_Specific_Populations_ENTRE, Use_in_Specific_Populations_ERLOT, Use_in_Specific_Populations_ETOP, Use_in_Specific_Populations_ETOPO, Use_in_Specific_Populations_EXKIV, Use_in_Specific_Populations_GAVRE, Use_in_Specific_Populations_GEFIT, Use_in_Specific_Populations_GEMZA,

Use_in_Specific_Populations_GILOT, Use_in_Specific_Populations_HYCAM, Use_in_Specific_Populations_IMFIN, Use_in_Specific_Populations_IMJUD, Use_in_Specific_Populations_INFUG, Use_in_Specific_Populations_IRESS, Use_in_Specific_Populations_KEYTR, Use_in_Specific_Populations_KRAZA, Use_in_Specific_Populations_LIBTA, Use_in_Specific_Populations_LORBR, Use_in_Specific_Populations_LUMAK, Use_in_Specific_Populations_LURB, Use_in_Specific_Populations_MEKIN, Use_in_Specific_Populations_METH, Use_in_Specific_Populations_MVASI, Use_in_Specific_Populations_OPDIV, Use_in_Specific_Populations_PORTR, Use_in_Specific_Populations_RAMUC, Use_in_Specific_Populations_RETEV, Use_in_Specific_Populations_ROZLY, Use_in_Specific_Populations_RYBRE, Use_in_Specific_Populations_SELPE, Use_in_Specific_Populations_SOTOR, Use_in_Specific_Populations_TABRE, Use_in_Specific_Populations_TAFIN, Use_in_Specific_Populations_TAGRIS, Use_in_Specific_Populations_TAXOT, Use_in_Specific_Populations_TECEN, Use_in_Specific_Populations_TEPME, Use_in_Specific_Populations_TOPO, Use_in_Specific_Populations_TRAME, Use_in_Specific_Populations_TREME, Use_in_Specific_Populations_TREXA, Use_in_Specific_Populations_VINOR, Use_in_Specific_Populations_VIZIM, Use_in_Specific_Populations_XALKO, Use_in_Specific_Populations_YERVO, Use_in_Specific_Populations_ZIRAB, Use_in_Specific_Populations_ZYKAD, Vinorelbine_Tartrate_, Warnings_and_Precautions_ABRAX, Warnings_and_Precautions_ADAGR, Warnings_and_Precautions_AFATI, Warnings_and_Precautions_AFINI, Warnings_and_Precautions_AFINIT, Warnings_and_Precautions_ALECE, Warnings_and_Precautions_ALIMT, Warnings_and_Precautions_ALUNB, Warnings_and_Precautions_ARYMS, Warnings_and_Precautions_AMIVA, Warnings_and_Precautions_ATEZO, Warnings_and_Precautions_AVAST, Warnings_and_Precautions_BRIGA, Warnings_and_Precautions_CAPMA, Warnings_and_Precautions_CEMIP, Warnings_and_Precautions_CYRAM, Warnings_and_Precautions_DOXOR, Warnings_and_Precautions_DURVA, Warnings_and_Precautions_ENHER, Warnings_and_Precautions_ENTRE, Warnings_and_Precautions_ERLOT, Warnings_and_Precautions_ETOP, Warnings_and_Precautions_ETOPO, Warnings_and_Precautions_EXKIV, Warnings_and_Precautions_GAVRE, Warnings_and_Precautions_GEFIT, Warnings_and_Precautions_GEMZA, Warnings_and_Precautions_GILOT, Warnings_and_Precautions_HYCAM, Warnings_and_Precautions_IMFIN, Warnings_and_Precautions_IMJUD, Warnings_and_Precautions_INFUG, Warnings_and_Precautions_IRESS, Warnings_and_Precautions_KEYTR, Warnings_and_Precautions_KRAZA, Warnings_and_Precautions_LIBTA, Warnings_and_Precautions_LORBR, Warnings_and_Precautions_LUMAK, Warnings_and_Precautions_LURB, Warnings_and_Precautions_MEKIN, Warnings_and_Precautions_METH, Warnings_and_Precautions_MVASI, Warnings_and_Precautions_OPDIV, Warnings_and_Precautions_PORTR, Warnings_and_Precautions_RAMUC, Warnings_and_Precautions_RETEV, Warnings_and_Precautions_ROZLY, Warnings_and_Precautions_RYBRE, Warnings_and_Precautions_SELPE, Warnings_and_Precautions_SOTOR, Warnings_and_Precautions_TABRE, Warnings_and_Precautions_TAFIN, Warnings_and_Precautions_TAGRIS, Warnings_and_Precautions_TAXOT, Warnings_and_Precautions_TECEN, Warnings_and_Precautions_TEPME, Warnings_and_Precautions_TOPO, Warnings_and_Precautions_TRAME, Warnings_and_Precautions_TREME, Warnings_and_Precautions_TREXA, Warnings_and_Precautions_VINOR, Warnings_and_Precautions_VIZIM, Warnings_and_Precautions_XALKO, Warnings_and_Precautions_YERVO, Warnings_and_Precautions_ZIRAB, Warnings_and_Precautions_ZYKAD

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