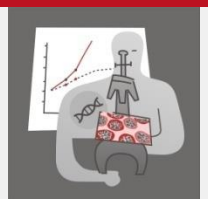
CURELINE GROUP:

Global Translational Research CRO Specializing in HBS Procurement, Analysis and Precision Medicine R&D Services



18 Years of
Human Tissue Excellence

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CURELINE GROUP: Global Presence (2003 – 2021)

- **700+ clients** worldwide (pharma/biotech, academia, government, hospitals)
- International Clinical Network Operations (**150+ centers, 20 countries**)
- Over **400 projects annually** (4,000+ completed)
- Effective regional and local **Distributors** (Japan, UK, EU, Asia/Pacific)
- **HQ in California** (USA) and worldwide clinical outreach

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CURELINE Group Services: Translational Medicine CRO and HBS Biobank

CURELINE (USA)

Translational Medicine CRO

Brisbane, CA, USA

HBS Tissue Bank (Cureline)

- Study Protocol Design
- Global Regulatory Affairs
- Global Clinical Network
- Clinical Trials Support
- Wide Range of HBS Collection
- Special Lab Processing Protocols
- HBS Storage and Distribution
- US Government Contracts

Translational Histopathology (CBP)

- Clinical Trial Support (Spec. protocols)
- Research Tissue Processing (animal, human)
- Special Stains
- Target expression & activation (IHC)
- Copy number analysis (FISH)
- Tissue Slide HD scanning
- Tissue Micro Arrays (TMA)
- Animal Toxicology Studies
- Pathology Report (USA)

Molecular Services (CMS), San Diego

- Molecular & Cellular assays
- Cell & Tissue culture
- DTC and 3D-histoculture (IO projects)
- Glycoproteome (BioCrypton™)
- Bioinformatics
- Blood processing & components

2003 – 2008 SERVICE DEVELOPMENT TIMELINE **2008 – 2020**

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CURELINE Competitive Advantages

- **World-class translational medicine and biobanking expertise**:
  - Founded in South San Francisco in **2003** by former **SUGEN**ites
  - Successful commercial biobanking operations for **17 years (700+ clients)**
  - Global clinical operations in **20 countries** with **130+ TSS** (clinical sites)
  - Excellence in global biobanking regulations and **regulatory compliance**
  - **Standardized biobanking protocols**, NCI/ISBER Best Biobanking Practices and CAP-spirited Quality Management system
- **Validated biotech/clinical Executive Management Team** with extensive expertise in Oncology, Inflammation, Diabetes, ID, CNS and other therapeutic areas. Currently 25+ highly qualified FTEs and 30+ consultants.
- **Excellent customer base**:
  - **24/30 top pharma, 6 top biotech** companies, Dx giants, major CROs, startups around the world
  - Multiple US government contracts:
    - contractor for **TCGA** (2010-2015) and **CPTAC** (2015-current) programs (NIH)
    - FDA and CDC: verified HBS supplier
  - Major league Universities (Stanford, Harvard, UCSF)
  - Distributors in global markets (Japan, UK, EU, Singapore)
- **Strategic geographical location** (San Francisco Bay Area, CA) and proximity to Silicon Valley with access to newest technology, experienced personnel and consultants, world-class academic collaborations, equipment, and local/international logistics

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Cureline Group Facilities

Cureline Group HQ currently occupies ~6,000SF of laboratory and office space in **Brisbane, CA** **(San Francisco Bay Area, USA)**

- Executive Offices and open office space with 12 work stations
- Life sciences laboratory dedicated to HBS tissue bank, including three areas with specific requirements:
  - **ULT storage/sorting laboratory** (LN2 storage area, -80C freezer area, frozen specimens sorting area and dedicated back-up generator).
  - **Ambient temperature HBS processing laboratory** (FFPE and slides storage and sorting area; collection kits and documentation area; shipping area).
- **Cureline Molecular Services** laboratory in **San Diego, CA** is dedicated to cell culture, tissue culture, DNA/RNA/Protein analyses, sequencing and other high-end scientific services. ~1,500SF lab/office.
- **Cureline BioPathology** is co-localized with Cureline and has specialized histology laboratory space for tissue processing and analyses (2 dedicated laboratory rooms).
- **BioCrypton** has an office and laboratory space, and conducts its laboratory operations from Cureline Group Headquarters.

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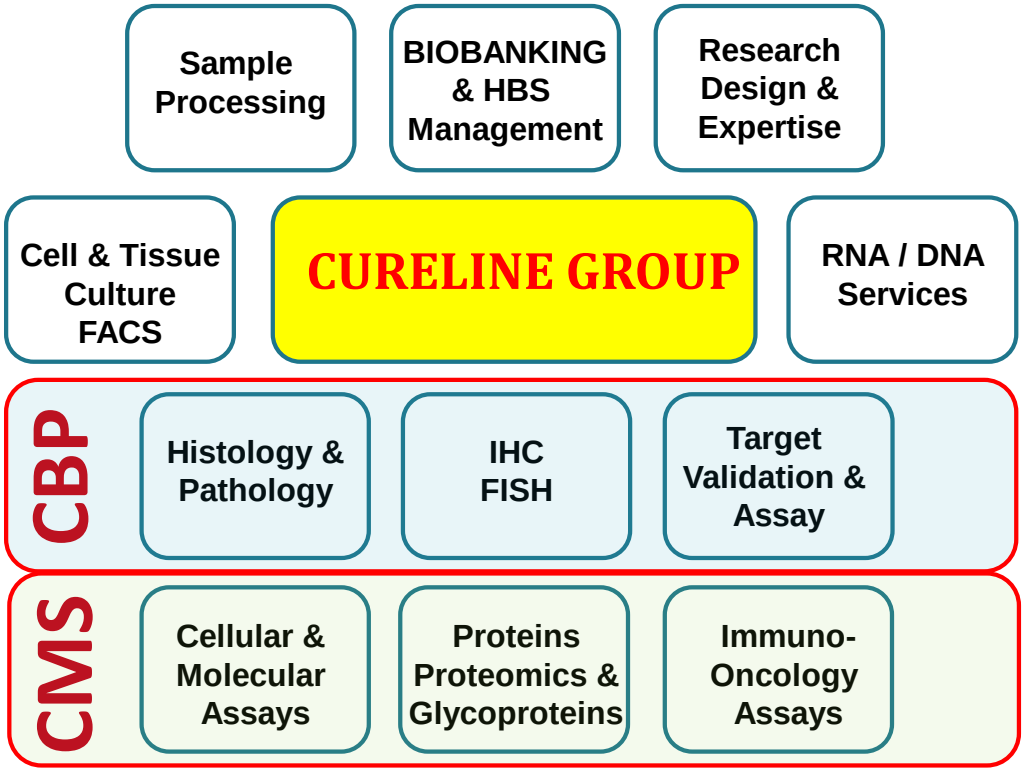
Unique Cureline Qualifications as a Fusion CRO

Human Biospecimens (HBS) and related services are offered with limited scope by biotech companies, CRO, CMO and laboratories.

CURELINE GROUP offers a unique range of services:

- Clinical study design
- Research protocol expertise
- Sample collection (biobanking)
- Sample management
- Sample Processing:
- Proteomics/glycoproteomics
- Molecular assays
- Cellular Assays
- Immuno-Oncology Assays
- Histology/pathology services
- Immunohistochemistry / FISH
- Target validation / assay
- Bioinformatics



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Outstanding Business Environment

Cureline HQ is located in the heart of the San Francisco Biotech Bay – one of the most advanced biotech hubs in the US and in the world

- The facilities of Cureline (human biobank), Cureline BioPathology (translational histopathology laboratory) and BioCrypton (diagnostics start-up) are located in the San Francisco Biotech Bay (California, USA) attracting big pharma, biotech, medical device and manufacturing organizations.

- San Francisco Biotech Bay is a center of the pharmaceutical industry in the US, providing a positive cluster environment and life sciences rich infrastructure that allows companies like Cureline Group to prosper.

- San Francisco International Airport (SFO) is within 10 minutes driving distance, providing easy access to the US, Europe and Asia based customers.

- Major academic institutions including Stanford University, Berkeley, and USCF (all are Cureline customers) are located within a radius of 10 – 20 miles, providing excellent access to expertise and future employees.

- San Francisco Bay area is a Birth Place of Biotech with over 400 life sciences companies residing here

Agilent
AMGEN
MERCK
23andMe
Roche
UCSF University of California San Francisco
Genentech
Pfizer
Celgene
GILEAD
NOVARTIS
Stanford University
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UAB CURELINE BALTIC

Cureline
BALTIC PRECLINICAL CRO

Cureline Partner Project in Lithuania

- **UAB Cureline Baltic** has been formed in April-2020 (Vilnius, LT)
- Company is currently located at the **Innovation Medicine Center** (IMC)
- Cureline Baltic **Team**:
  - Olga Potapova, PhD – CEO and Scientific Director
  - Agne Vaitkeviciene, MS – Chief Operating Officer
  - Laura Korsakova - DPharm, PhD candidate (2021)
- **Company focus**: preclinical project management with an emphasis on human sample validation studies for drug R&D and Dx development
- **CRO Services**: EU regulatory affairs, study design, HBS procurement and analyses, international scientific and commercial projects coordination

Olga Potapova, PhD

Founder, CEO and Scientific Director, Cureline
TCGA and CPTAC Principal Investigator

- 25+ years of leadership in research (genetics, signal transduction in aging and cancer, diagnostics, translational & precision medicine)
- International recognition in the fields of biobanking, laboratory service, and management of multinational pre/clinical research projects
- Academic, biotech and big pharma R&D experience
- Excellence in translational medicine and drug development (SUTENT)
- Founder and CEO of Cureline, Inc., since 2003
- Co-Founder and Managing Partner of Cureline BioPathology LLC since 2008
- TCGA and CPTAC Principal Investigator since 2010
- President of BioCrypton, Inc., since 2014
- Managing Partner of Cureline Molecular Services LLC, since 2019

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I. CURELINE Expertise: Biobanking

- **Custom HBS acquisition study design and implementation:**
  - Precision medicine (therapeutics, molecular and companion Dx)
  - Biomedical research (commercial and academic)
  - Medical devices (assay design, validation studies, clinical trials)
- **California-based biorepository (San Francisco Bay area):**
  - About **50,000 samples** (LN2, -80C freezers, controlled ambient temperature)
  - **7,000 individual** clinically-defined **cases**
  - Comprehensive de-identified clinical data for each clinical case
  - Wide range of specimens formats: tissues, biofluids, cells, etc.
  - Major therapeutic areas: Oncology, Immunology/AID, ID, CV, etc.
  - FDA-compliant databases (FreezerWorks/Pro, PathXL, CITRIX medfiles)
- **17 years of expertise** in commercial biobanking for precision medicine:
  - Targeted therapeutic research and development
  - Biomarkers discovery and development
  - Molecular Dx and Companion Diagnostics (CDx) development
  - Clinical trial support: IHC assay development (CBP), biospecimens collection, protocol / SOP development, site management (selection, training, monitoring)

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II. CURELINE Expertise: HBS Management

- **Sample Management Consulting:** resources, processes, technology, equipment and infrastructure evaluation and advise
- **Sample Management Solutions:** control, compliance and cost-saving
  - Sample storage: long- and short-term solutions, secure location, controlled temperature options: RT, 2-8C, -20C,-80C, -190C (LN2)
  - Sample inventory management: server- and web-based 21 CFR Part21 compliant DB options for fast and secure control of clients' HBS information
    - Individual login/authorization/access options
  - Sample Distribution: retrieval and shipment by client request; qualified transportation services (IATA and US DOT trained and certified personnel)
- **Laboratory Services** (sample preparation):
  - Transfer into desired matrix components:
    - blood derivatives: serum, plasma, PBMC;
    - molecular analytes: DNA, RNA, protein (extraction and verification)
  - Volumetric and normalized aliquoitng
  - OCT and FFPE tissues blocks and slides preparation
  - Pathology assessment and QC
  - HD image scan and analysis
- **Clinical Trials support:** Collection kits (design, labels design/printing, ordering, TSS training, delivery); site management; HBS receiving, processing and management.

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III. CURELINE Immuno-Oncology Services

- **3D histoculture** – investigation of drug effects in fresh human tumor prepared *ex-vivo* for 12-48 hours culture
  - FFPE and/or FF tumor tissue (RNA, DNA, morphology, IHC)
  - Frozen culture supernatant (cytokines expression analysis)
- **"Tumor soup"** – preparation of dissociated tumor cells (DTC) from an individual human tumor (cancer cells, stromal cells, inflammatory components)
  - Viable cell in DMSO-containing media
- **PDx Models (viable tumor pieces)** – investigation of drug response *in vivo* (modeling of multiple human tumor types in mice)
  - Primary human tumor fragments frozen in DMSO-containing media
  - Human xenografts from mice frozen in DMSO-containing media
- **Matching Oncology HBS Sets** – correlative investigation of Biomarkers and Immune-specific events
  - LBx (serum, plasma; standard & special protocols)
  - PBMC (viable preparation, within 2 – 4h post blood draw)
  - Tumor tissue (FF, FFPE, viable prepapation)

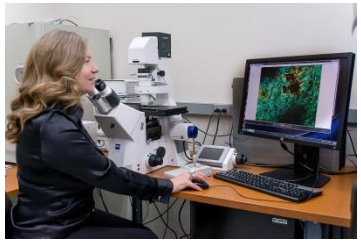
Cureline
HUMAN BIOSPECIMEN CRO

IV. Cureline BioPathology (CBP) Services

- **Standard histology:**
  - Wet tissue processing
  - Tissue sections (FFPE/OCT)
  - Tissue curls (sterile/RNA)
  - H&E and special stains
- **Special Stains**
  - Normal Human Tissues
  - Hematology (blood and BM)
- **Cross-Reactivity (FDA, IMEA)**
  - Rapid autopsy (2 – 6 h PMI)
  - Fresh-frozen (FF) and OCT
  - Fixed (FFPE blocks)
  - Antibody cross-reactivity
- **IHC & FISH**
  - Target expression / activation
  - 100+ standard protocols
  - Custom Ab assay development
  - Fluorescent staining and image analysis (Zeiss)
  - Biomarker assay development

- **TMA: Cancer and Normal Human Tissues**
  - Thousands samples ready to go
  - Custom selection
  - Custom acquisition (Cureline)
  - Various TMA design parameters
  - Pathologist review / area selection
  - Semi-automated printing
  - H&E slides preparation
  - IHC staining + image/HD scan
- **Special protocol development** for human tissue processing in clinical trials (Phase II): Collaborative efforts with Trial Sponsor, Clinical Network, Academic Investigators, Manufacturer
- Special equipment / reagents
- IHC / FISH staining + image/HD scan
- **Digital pathology** and image analysis
- Pathology report (USA)

V. Cureline Molecular Services (CMS)



- **HBS Collection and Preparation for All Studies:**
  - Consulting on a study design (HBS use for R&D and validation studies)
  - Transfer of CTB and Customer samples into desired matrix components:
    - blood derivatives: serum, plasma, PBMC, BMMC
    - molecular analytes: DNA, RNA, protein (extraction and verification)
    - Stem / Progenitor cells isolation from fresh lipoaspirate
    - 3D-Histoculture and DTC for Immuno-Oncology studies
  - Volumetric and normalized aliquoting
- **Biomarker Discovery and Validation:**
  - Nucleic Acids (RNA, DNA, cfDNA, microRNA, etc.)
  - Cell-based assays (all kinds)
  - Molecular profiling for mutation panels and Case ID
- **Proteomic Studies:**
  - Protein lysate and fractions isolation, QC and analyses
  - Protein array (reverse phase)
  - Total proteome (LC-MS)
  - Glycoproteome (BioCrypton™)
- **Custom Protocols**
  - ELISA & Antibody characterization
  - Molecular and Cellular Biology