

# Index

## A

AA. *See* Aplastic anemia

*ABL1*, 347, 368–369

*ABL2*, 369

ABT-199, 368

ABT-731, 181

*ACIN1*, 374

Acute lymphocytic leukemia (ALL). *See also* B-

progenitor acute lymphoblastic leukemia; T-cell acute lymphoblastic leukemia

epidemiology

adult, 32–33

pediatric, 29–30

Acute megakaryoblastic leukemia (AMKL)

children without Down syndrome, 326–329

Down syndrome association

clinical and biological features, 324–325

*GATA1*

cooperation with trisomy genes, 323–324

mutations, 323

genetic susceptibility, 321–322

transforming mutation acquisition, 325–326

overview, 319–320

RNA-binding proteins, 153

Acute myeloid leukemia (AML)

chromosomal abnormalities

core binding factor rearrangements, 296–297

*KMT2A* rearrangements, 298–299

rare translocations, 299–300

clonal hematopoiesis, 75

epidemiology

adult, 31–32

pediatric, 29–31

epigenetics

cytosine methylation profiles, 115–117

gene mutations

*ASXL1*, 120–121, 306

*BCOR*, 306–307

*BCORL1*, 306–307

cohesin, 307

*DNMT3A*, 117, 304–305

*EZH2*, 120

*IDH1*, 120, 305–306

*IDH2*, 120, 305–306

*LUC7L2*, 307

*PRPF8*, 307

*SF3B1*, 307

*SRSF2*, 307

*SUZ12*, 120

*TET2*, 117, 119, 121, 305

*U2AF1*, 307

*U2AF2*, 307

*ZRSR2*, 307

therapeutic targeting

combination therapy, 123–124

histone epigenetic mechanisms, 121, 123

specific epigenetic mechanisms, 121

induced pluripotent stem cell models, 257–259

leukemia stem cell studies. *See* Leukemia stem cell model

mouse models. *See* Mouse models

pathophysiology, 295–296

recurrent mutations

*CEBPA*, 301–302

*GATA2*, 302

*NPM1*, 300–301

*RUNX1*, 301

signal transduction mutations

*CBL*, 303

*FLT3*, 302

*KIT*, 302–303

*KRAS*, 303

*NFI*, 303–304

*NRAS*, 303

*PTPN11*, 303

therapeutic targeting

*CD123*, 91–92

*CD33*, 90

*FLT3*, 90–91

limitations, 90

prospective leukemia stem cell targets.

*See* Leukemia stem cell

tumor suppressor gene mutations

*PHF6*, 308

*TP53*, 307–308

*WT1*, 308

*ADI-PEG20*, 182

Adult T-cell leukemia/lymphoma (ATLL)

clinical presentation, 473–474

genetics, 474

pathogenesis, 473

## Index

- AF10*, 298  
*AF4*, 298  
*AF9*, 298, 303  
Age-related clonal hematopoiesis (ARCH), 11, 13, 73  
*AICDA*, 49  
*AITL*. *See* Angioimmunoblastic T-cell lymphoma  
*AKT*, 346  
*ALCL*. *See* Anaplastic large cell lymphoma  
*Alisertib*, 329  
*ALK*, 431  
*ALK*, 55–56, 473  
*ALL*. *See* Acute lymphocytic leukemia  
*AMKL*. *See* Acute megakaryoblastic leukemia  
*AML*. *See* Acute myeloid leukemia  
*AML1*, 303  
*AMPK*, 7  
Anaplastic large cell lymphoma (ALCL)  
    clinical features, 472  
    genetics, 472–473  
    genetics, 55–56, 472–473  
    overview, 187  
*Angioimmunoblastic T-cell lymphoma (AITL)*  
    epidemiology, 469  
    genetics, 57 469–471  
*APC*, 326, 471  
*Aplastic anemia (AA)*, 74  
*APOBEC*, 119  
*ARAF*, 425  
*ARCH*. *See* Age-related clonal hematopoiesis  
*ARF*, 340  
*ARHGEF1*, 240  
*ARID1A*, 51, 54, 476  
*ARID1B*, 475  
*ARID1B*, 471  
*ARID2*, 283  
*ARID2*, 471  
*ARID5B*, 476  
*ASCT2*, 181  
*ASNS*, 181  
*ASS1*, 182  
*ASXL1*, 70, 74, 120–121, 260, 280–281, 302, 306  
*ATLL*. *See* Adult T-cell leukemia/lymphoma  
*ATM*, 49, 243, 451, 454  
*ATR*, 128  
*AURKA*, 329
- B**
- Bach2*, 206  
*B-ALL*. *See* B-progenitor acute lymphoblastic leukemia  
*BAP1*, 306  
*BAX*, 186, 456  
*BCAT1*, 159, 184  
*B-cell*, development, 226–227, 448–449
- B-cell lymphoma*. *See also* specific lymphomas  
    classification, 448, 451  
    genetics, 450–451  
    germinal center B-cell-derived lymphomas, 451–452  
    lymphomagenesis, 448  
    post-germinal center and marginal zone B-cell-derived lymphomas, 452–453  
    pre-germinal center B-cell-derived lymphomas, 451  
*B-cell maturation antigen (BCMA)*, 494–497  
*BCL1*. *See* *CCND1*  
*BCL2*, 49, 152, 183, 185, 368, 396, 399  
*BCL2L*, 52, 54, 162, 234–236, 239, 374, 448, 452  
*BCL6*, 128, 236–237, 239, 242, 306  
*BCL6*, 52, 54, 374, 452  
*BCL11B*, 342, 344  
*BCMA*. *See* B-cell maturation antigen  
*BCOR*, 74, 306–307  
*BCORL1*, 74, 306–307  
*BCR*, 368–369  
*BHLHB1*, 341  
Bioenergetics. *See* Metabolism, leukemia/lymphoma  
*BIRC3*, 389  
*BiTEs*, 495–497  
*BL*. *See* Burkitt lymphoma  
*BLCL2A1*, 186  
*BLIMPI*, 241  
*BMI1*, 152, 161  
*Bortezomib*, 478, 489  
*B-progenitor acute lymphoblastic leukemia (B-ALL)*  
    chromosomal alterations  
        gross abnormalities, 364, 367  
        translocations, 367–368  
    inherited variants, 375–376  
    microenvironment, 377  
    mixed phenotype ALL, 374–375  
    overview, 363–364  
    prospects for study, 377–378  
    relapse, 376–377  
    subtypes  
        DUX4-rearranged ALL, 371  
        ETV6-RUNX1-like ALL, 369  
        IGH rearrangements, 374  
        IKZF1 N159Y, 372, 374  
        MEF2D rearrangement, 371  
        novel subtypes, 368–372  
        NUTM1 rearrangements, 374  
        PAX5-driven subtypes, 372  
        Ph-like ALL, 369  
        prevalence and prognosis, 365–366  
        ZNF384 rearrangement, 371–372  
*BRAF*, 425, 439, 492  
*BRAF*, 51, 53, 59, 421–423, 430–433, 437–440  
*BRD4*, 281  
*BRD4*, 374

- BRD9*, 374  
Brentuximab, 456  
*BTK*, 49, 403, 456  
*BTK*, 50  
*BTLA*, 364  
Burkitt lymphoma (BL)  
  genetics, 54  
  mouse models, 232–233
- C**
- CALR*, 257, 276  
*CARD11*, 56, 457, 476  
Carfilzomib, 488  
*CBCL*. *See* Primary cutaneous B-cell lymphoma  
*CBFA2T3*, 328–329  
*CBFB*, 296–297  
*CBL*, 284  
*CBL*, 70, 284–285, 303  
*CCL3*, 393  
*CCL4*, 393  
*CCND1*, 50, 52, 229, 451  
*CCND2*, 341  
*CCND3*, 51, 54, 233, 338, 340, 439  
*CCR4*, 474, 479  
*CCR4*, 57  
*CCR7*, 474  
*CCUS*. *See* Clonal cytopenia of undetermined significance  
*CD3*, 348  
*CD7*, 348  
*CD19*, 458  
*CD200*, 364  
*CD23*, 395  
*CD28*, 471, 474  
*CD30*, 480  
*CD31*, 393  
*CD33*, 90  
*CD38*, 392–393, 395, 491, 493, 497  
*CD47*, 479  
*CD58*, 474  
*CD79B*, 452–453  
*CD123*, 91–92  
*CDK4*, 232  
*CDK4*, 338  
*CDK6*, 338  
*CDKN1A*, 237  
*CDKN1B*, 237, 340, 476  
*CDKN2A*, 56, 337, 340, 364, 368, 375  
*CDKN2B*, 364, 368, 375  
*CDKN2D*, 338  
*CDR*, 242  
*C/EBP*, 159–160  
*CEBPA*, 301–302
- CFS1R*, 371  
CH. *See* Clonal hematopoiesis  
*CHAF1B*, 322  
*CHD8*, 471  
*CHEK1*, 128  
*CHIP*, 276  
Chronic lymphocytic leukemia (CLL)  
  B-cell surface receptors  
    B-cell receptor signaling, 390–392  
    chemokine receptors, 392  
    microenvironmental signals associated with clonal expansion, 392–393  
  combinatorial indices in management, 396  
  diagnosis, 395  
  epidemiology, 386  
  genetics  
    noninherited recurrent mutations, 388–390  
    susceptibility genes, 386, 388  
  monoclonal B-cell lymphocytosis, 393–394  
  normal cell equivalents, 394–395  
  overview, 385–386  
  predictive markers in therapy, 395–396  
  prognostic markers, 395  
  progression  
    aggressive clonal variant promoters, 399  
    cell growth rate role, 400  
    clonal evolution, 400  
    Richter’s transformation, 400, 402–403  
  risk factors, 386  
  treatment  
    anti-apoptotic protein targeting, 399  
    chemoimmunotherapy, 398  
    initial therapy, 396–397  
    monoclonal antibodies, 398  
    pathway inhibitors, 398–399  
    progression targeting, 403  
    refractory disease, 402–403  
    relapsed disease, 402–403  
Chronic Lymphocytic Leukemia International Prognostic Index (CLL-IPI), 396  
Chronic lymphocytic leukemia/small cell lymphoma (CLL/SCL)  
  epidemiology, 33–34  
  genetics, 48–50  
  mouse models, 242–243  
Chronic myeloid leukemia (CML)  
  epidemiology, 33  
  induced pluripotent stem cell models, 255–256  
CLL. *See* Chronic lymphocytic leukemia  
CLL/SCL. *See* Chronic lymphocytic leukemia/small cell lymphoma  
CLL-1, acute myeloid leukemia therapeutic targeting, 101–102

## Index

- CLL-IPI. *See* Chronic Lymphocytic Leukemia International Prognostic Index
- Clonal cytopenia of undetermined significance (CCUS), 73–74
- Clonal hematopoiesis (CH)  
  aplastic anemia, 74  
  bystander clonal hematopoiesis, 75–76  
  clonal cytopenia of undetermined significance, 73–74  
  founder clonal hematopoiesis and leukemia progression, 74–75  
  genetic susceptibility, 77  
  hematologic malignancy risk, 71  
  idiopathic cytopenia of undetermined significance, 73–74
- interventions  
  follow-up, 78  
  inflammation inhibition, 78  
  metformin, 78  
  mutation targeting, 77  
  preclinical studies, 77  
  vitamin C, 77–78
- multiple myeloma outcomes, 76
- mutation landscape, 70–71
- overview, 69–70
- prospects for study, 78–79
- solid tumor outcomes, 76
- technical definition, 71–73
- CML. *See* Chronic myeloid leukemia
- CNOT3, 348
- Cohesin, 214, 255, 307
- CPI-613, 180
- CREBBP, 234–237
- CREBBP, 52, 53, 128–130, 364, 452, 471
- CRISPR–Cas9, 204–205, 244, 255, 258, 460
- Crizotinib, 479
- CRLF2, 367, 369, 374
- CSF1R, 432
- CTCF, 214, 329
- CTCF, 329
- CTCL. *See* Cutaneous T-cell lymphoma
- CTLA4, 496
- Cutaneous T-cell lymphoma (CTCL)  
  clinical presentation, 476  
  genetics, 476
- CUX1, 374
- CXCL12, 4–5, 206, 337, 392
- CXCR4, 206, 337, 377, 392
- CXCR4, 453
- D**
- Daratumumab, 488
- DCAF15, 160–161
- DDX3X, 452
- E**
- DEK, 299
- D2HGDH, 188
- DHODH, 183
- Diffuse large B-cell lymphoma (DLBCL)  
  cellular origins, 228  
  epidemiology, 37–38  
  epigenetics  
    cytosine methylation patterning, 130  
    gene mutations in epigenetic modifiers, 128–130  
  immune synapse as focal point for epigenetic dysregulation in lymphoma, 130  
  overview, 124–128  
  therapeutic targeting  
    nonspecific therapies, 130, 132  
    precision therapy, 132–133
- genetics, 52–54, 451–452
- heterogeneity, 460–461
- mouse models  
  BCL6 dysregulation, 239  
   $FBXO11$  deletion, 240  
  Gα13 pathway disruption, 240  
  NF-κB signaling activation, 241–242  
   $PRDM1/BLIMPI$ , 241
- DLBCL. *See* Diffuse large B-cell lymphoma
- DLEU2, 242
- DLEU7, 242
- DNA methyltransferase. *See also* Epigenetics  
  acute myeloid leukemia inhibitor therapy, 124  
  DNMT1, 279  
  DNAMT3A, 13–14, 57, 70, 74–75, 77–78, 85, 117, 206, 210–211, 260, 279–280, 304–305, 319, 469, 476
- DOT1L, 298–299
- Down syndrome  
  acute megakaryoblastic leukemia  
  clinical and biological features, 324–325  
  GATA1  
    cooperation with trisomy genes, 323–324  
    mutations, 323  
  genetic susceptibility, 321–322  
  transforming mutation acquisition, 325–326  
  hematopoiesis disturbances, 321  
  malignancy association, 320–321
- Durvalumab, 480
- DUSP22, 56
- DUX4, 368, 371
- DYRK1A, 324
- DYRK1A, 367

- 4EBP1, 161–162  
EBV. *See* Epstein–Barr virus  
ECD. *See* Erdheim–Chester disease  
EED, 345  
eIF4E, 155–157, 161  
eIF4G, 161  
*ELL*, 298  
*ENL*, 298  
Enteropathy-associated T-cell lymphoma (EATL), 475  
*EP300*, 52–53, 128–129  
Epigenetics  
    acute myeloid leukemia  
    cytosine methylation profiles, 115–117  
    gene mutations  
        *ASXL1*, 120–121, 306  
        *BCOR*, 306–307  
        *BCORL1*, 306–307  
        cohesin, 307  
        *DNMT3A*, 117, 304–305  
        *EZH2*, 120  
        *IDH1*, 120, 305–306  
        *IDH2*, 120, 305–306  
        *LUC7L2*, 307  
        *PRPF8*, 307  
        *SF3B1*, 307  
        *SRSF2*, 307  
        *SUZ12*, 120  
        *TET2*, 117, 119, 121, 305  
        *U2AF1*, 307  
        *U2AF2*, 307  
        *ZRSR2*, 307  
    therapeutic targeting  
        combination therapy, 123–124  
        histone epigenetic mechanisms, 121, 123  
        specific epigenetic mechanisms, 121  
B-cell lymphomas  
    cytosine methylation patterning, 130  
    gene mutations in epigenetic modifiers, 128–130  
    immune synapse as focal point for epigenetic dysregulation in lymphoma, 130  
    overview, 124–128  
    therapeutic targeting  
        nonspecific therapies, 130, 132  
        precision therapy, 132–133  
epigenetic alleles, clonal evolution and therapy  
    resistance in leukemia/lymphoma, 133  
mouse models of myeloid malignancies  
    DNA methylation pathways, 209–212  
    histone modification pathways, 212–213  
T-cell acute lymphoblastic leukemia regulator mutations  
    *EED*, 345  
    *EZH2*, 345  
    *KDM6A*, 345  
    overview, 344–345  
    *PHP6*, 345  
    *SUZ12*, 345  
Epstein–Barr virus (EBV)  
    Burkitt lymphoma association, 232  
    Hodgkin’s lymphoma association, 39  
    non-Hodgkin’s lymphoma association, 37  
*ERBB3*, 431  
Erdheim–Chester disease (ECD)  
    cellular origins, 432–433  
    clinical presentation, 430  
    immunophenotypic features, 429  
    treatment, 433–435  
*ERG*, 263–264, 321–322, 324–325, 367–368, 371, 375  
*ERK*, isoforms, 431  
*ETO*, 303  
*ETS2*, 321–322, 324  
*ETV3*, 432  
*ETV6*, 259  
*ETV6*, 336, 343, 364, 367–369, 375, 452  
Everolimus, 478  
*EVI1*, 182  
*EVI1*, 299–300  
*EZH2*, 132, 213, 234, 236–237, 239, 282–283, 457–458  
*EZH2*, 52, 56, 120, 128–129, 255, 257, 260, 281, 319, 326, 336, 345, 452
- F**
- FAS*, 474  
*FASN*, 182  
Fatty acid oxidation. *See* Metabolism, leukemia/lymphoma  
*FBXO11*, 240  
*FBXO11*, 240  
*FBXW7*, 474  
*FBXW7*, 338–339, 389  
FL. *See* Follicular lymphoma  
*FLT3*, 14, 90–91, 124, 159, 178, 181  
*FLT3*, 75, 205–207, 214, 302, 308, 336, 367–368, 372  
Follicular lymphoma (FL)  
    epigenetics  
        cytosine methylation patterning, 130  
        gene mutations in epigenetic modifiers, 128–130  
        immune synapse as focal point for epigenetic dysregulation in lymphoma, 130  
    overview, 124–128  
    therapeutic targeting  
        nonspecific therapies, 130, 132  
        precision therapy, 132–133  
genetics, 51–52, 452  
mouse models

## Index

- Follicular lymphoma (FL) (*Continued*)  
    *BCL2* translocation, 234–235  
    histone modification genes, 235–237  
    *MEF2B*-activating mutations, 238–239  
    overview, 233–234  
    *RRAGC* mutations, 238  
    *TNFRSF14* loss, 237–238
- Follicular T-cell lymphoma (FTCL), genetics, 57
- FOXO1, 233
- FOXO3, 6
- FOXP1, 453
- FTCL. *See* Follicular T-cell lymphoma
- FTO, 152
- G**
- Gα13*, 240
- GATA1*, 319–326, 329
- GATA2*, 326
- GATA2*, 257, 259, 299, 302
- GATA3*, 336, 344, 375, 472, 474
- GLIS2*, 328–329
- GLOBOCAN, 26, 35
- GLUT1, 184–185
- GLUT5, 178
- Glycolysis. *See* Metabolism, leukemia/lymphoma
- GNA13*, 239–240, 452
- H**
- Hairy cell leukemia (HCL)  
    cellular origin, 437–438  
    clinical presentation, 435–437  
    genetics, 51  
    pathophysiology  
        gene expression and methylation profiling, 437  
        genomic profiling, 435  
    treatment  
        chemotherapy, 438  
        targeted therapy, 438–439  
        vemurafenib resistance mechanisms, 439
- HBZ*, 473
- HCL. *See* Hairy cell leukemia
- HDAC. *See* Histone deacetylase
- Hematopoiesis. *See also* Clonal hematopoiesis  
    age-related clonal hematopoiesis, 11, 13, 73  
    demand-based hematopoiesis  
        inflammatory signals and hematopoietic regeneration, 8–9  
    lineage bias and reprogramming during emergency hematopoiesis, 7–8  
    pathogen response, 9–10  
    resolution of emergency hematopoiesis, 10
- Down syndrome disturbances, 321
- GATA1 role, 322–323
- overview, 1–2
- Hematopoietic stem cell (HSC)  
    DNA damage and functional decline, 5–6  
    early function disruption in acute myeloid leukemia, 87–88  
    lineage commitment, 3–4  
    malignancy  
        dysregulated self-renewal in clonal hematopoiesis and malignancy, 11–14  
    overview, 11  
    regenerative pathway activation, 14  
    metabolism and activation, 6–7  
    multipotency, 2–3  
    niche, 4–5
- Hepatosplenic T-cell lymphoma (HSTCL), 475
- HES1*, 338, 340
- HGBL. *See* High-grade B-cell lymphoma
- High-grade B-cell lymphoma (HGBL), genetics, 54–55
- HIPK2*, 257
- Histone deacetylase (HDAC)  
    *HDAC3*, 236  
    *HDAC9*, 371  
    inhibitors, 477, 480
- HIV. *See* Human immunodeficiency virus
- HL. *See* Hodgkin's lymphoma
- HLF*, 368
- HMGA2*, 154
- HMG-CoA* reductase, 182
- HNRNPA3*, 164
- hnRNPk*, 159–160
- HNRNPR*, 164
- Hodgkin's lymphoma (HL)  
    epidemiology, 38–39  
    genetics, 55
- HOXA*, 206, 300, 336
- HOXA5*, 264
- HOXA9*, 158–159, 161, 263–264
- HOXA9*, 298, 342
- HOXA10*, 342
- HOXB*, 206, 300
- HOXD13*, 209
- Hprt*, 207
- HRAS*, 347
- HSC. *See* Hematopoietic stem cell
- HSTCL. *See* Hepatosplenic T-cell lymphoma
- HTLV-1, 473
- Human immunodeficiency virus (HIV)  
    Hodgkin's lymphoma association, 39  
    immunodeficiency-related lymphoma, 453–454  
    non-Hodgkin's lymphoma association, 36–37
- HuR*, 155–156

I

Ibrutinib, 456  
ICH. *See* Indeterminate cell histiocytosis  
ICUS. *See* Idiopathic cytopenia of undetermined significance  
ID3, 232  
ID3, 54, 452  
IDH, 186–188  
IDH1, 13  
*IDH1*, 77, 120, 210, 212, 259, 279, 305–306  
*IDH2*, 13, 57, 77, 120, 210, 212, 259, 279, 305–306, 336, 469–470  
Idiopathic cytopenia of undetermined significance (ICUS), 73–74  
IGF2BP1, 157–158  
IGF2BP2, 157  
IGF2BP3, 157–158  
IGFBP1, 178  
IGFBP7, 157  
*IGH*, 369, 371, 452–563  
*IGHD*, 389–390, 394, 399  
*IGHJ*, 389–390, 394, 399  
*IGHV*, 389–389, 394, 396, 398–399  
IGK, 452  
IGL, 452  
IKZF1, 178, 491, 493  
*IKZF1*, 364, 368–369, 372, 374–375, 377  
IKZF3, 491, 493  
IL1RAP, acute myeloid leukemia therapeutic targeting, 102–104  
IL7R, 346–347  
IL7R, 367, 369  
IMPDH, 183  
Indeterminate cell histiocytosis (ICH)  
  cellular origins, 432–433  
  clinical presentation, 430  
  immunophenotypic features, 429  
  treatment, 433–435  
Induced pluripotent stem cell (iPSC)  
  comparison to other patient-derived models, 260–261  
  CRISPR–Cas9, 255  
  developmental stage and impact on disease modeling, 262  
  genetic stability, 261–262  
  good practices, 263  
  hematopoietic specification, 253–255  
  leukemia/lymphoma models, 255–259  
  line-to-line variation, 262–263  
  overview, 251  
  prospects  
    expandable hematopoietic precursors, 263–264  
    leukemia studies, 259–260

three-dimensional culture, 264

transplantable cells, 264

reprogramming malignant cells, 251–253

INO80, 475

iPSC. *See* Induced pluripotent stem cell

*IRF4*, 237, 243, 474

*IRF4*, 241

Isatuximab, 490

*ITD*, 302–303, 308

Ixazomib, 488, 490

*IZKF2*, 474

J

*JAK1*, 8

*JAK1*, 56, 369, 472, 476

*JAK2*, 14, 284, 286–287, 456

*JAK2*, 55, 70, 74, 77, 257, 272, 276, 278, 326

*JAK3*, 56, 369, 432, 476

JARID1A, 328

JMML. *See* Juvenile myelomonocytic leukemia

Juvenile myelomonocytic leukemia (JMML), induced pluripotent stem cell models, 257

Juvenile/adult xanthogranuloma (JXG/AXG)

  cellular origins, 432–433

  clinical presentation, 429

  immunophenotypic features, 429

  treatment, 433–435

JXG/AXG. *See* Juvenile/adult xanthogranuloma

K

*KDM5A*, 328

*KDM6A*, 345, 377, 471

*KIT*, 302–303

*KLF2*, 51, 435

*KMT2A*, 121, 123, 213, 328

*KMT2A*, 298–299, 368, 374

*KMT2C*, 451, 471

*KMT2D*, 234–236

*KMT2D*, 52–3, 128, 130, 452, 471

*KRAS*, 154, 492–493

*KRAS*, 205, 207–209, 285, 303, 347, 364, 433, 439

L

Langerhans cell histiocytosis (LCH)

  cellular origins, 432–433

  clinical presentation, 423, 428

  history of study, 423

  immunophenotypic features, 429

  treatment, 433–435

LCH. *See* Langerhans cell histiocytosis

LCOR, 264

LDHA, 184

## Index

- LEF1*, 344  
Lenalidomide, 488, 490  
Leukemia  
  epidemiology  
    acute lymphocytic leukemia, 32–33  
    acute myeloid leukemia, 31–32  
    chronic lymphocytic leukemia/small cell  
      lymphoma, 33–34  
    chronic myeloid leukemia, 33  
    global, 26  
    pediatric leukemia, 29–31  
    risk factors, 29  
    United States, 26–29  
  genetics. *See specific leukemias*  
Leukemia stem cell (LSC)  
  acute myeloid leukemia therapeutic targeting  
    CLL-1, 101–102  
    IL1RAP, 102–104  
    immunophenotype, 92  
    normal antigen expression, 93–97  
    prospects, 104  
    target functionality, 93  
    targeting strategy, 100  
    TIM-3, 100–101  
    timing of mutations, 93  
    unique antigens, 98–99  
cell origin for acute myeloid leukemia  
  cytogenetics studies, 84  
  functional heterogeneity in acute myeloid  
    leukemia organization, 89  
gene expression studies, 85  
hematopoietic stem cell function  
  disruption, 87–88  
mouse modeling of pre-leukemia, 84–85  
  sequencing studies, 85–87  
overview of model, 83–84  
relapse contribution, 89–90  
*LIN28*, 161  
*LIN28A*, 154–155  
*LIN28B*, 154–155  
*LKB1*, 7  
*LMO1*, 336, 341  
*LMO2*, 336, 341  
*LNK*, 284  
*LPL*. *See Lymphoplasmacytic lymphoma*  
*LSC*. *See Leukemia stem cell*  
*LUC7L2*, 257, 307  
*LYL1*, 336, 341  
Lymphoma  
  clinical genomics, 58–59  
  epidemiology  
    chronic lymphocytic leukemia/small cell  
      lymphoma, 33–34  
    Hodgkin's lymphoma, 38–39  
    non-Hodgkin's lymphoma, 35–38  
  genetics. *See specific lymphomas*  
Lymphoplasmacytic lymphoma (LPL), genetics, 51  
*LYN*, 369
- M**
- MAML1*, 340  
Mantle cell lymphoma (MCL)  
  cellular origins, 228  
  genetics, 50, 451  
  mouse models, 229–232  
*MAP2K1*, 51–52, 423, 431, 435, 440  
*MAP2K2*, 431  
MAPK mutations. *See Erdheim–Chester disease; Hairy cell leukemia; Indeterminate cell histiocytosis; Juvenile/adult xanthogranuloma; Langerhans cell histiocytosis; Rosai–Dorfman–Destombes disease; specific kinases*  
*MAPK1*, 451  
*MBD4*, 77  
MBL. *See Monoclonal B-cell lymphocytosis*  
MCL. *See Mantle cell lymphoma*  
*MCL1*, 49  
*MDR*, 242  
MDS, induced pluripotent stem cell models, 257–259  
*MEF2B*, 238–239  
*MEF2B*, 234, 238–239  
*MEF2C*, 298  
*MEF2D*, 368, 371  
*MEIS1*, 298  
*MEIS1*, 300  
MEITL. *See Monomorphic epitheliotropic intestinal T-cell lymphoma*  
Metabolism, leukemia/lymphoma  
  bioenergetics  
    leukemia  
      fatty acid oxidation, 180  
      glycolysis, 178–179  
      oxidative phosphorylation, 179–180  
    lymphoma  
      glycolysis, 184–185  
      oxidative phosphorylation, 185  
biomass  
  leukemia  
    amino acids, 181–182  
    lipids, 182  
    nucleotides, 183  
  lymphoma  
    amino acids, 185–186  
    lipids, 186–187  
    nucleotides, 187

- differentiation  
leukemia, 183–184  
lymphoma, 188  
overview, 173–178  
prospects for study, 188–189
- Metformin, clonal hematopoiesis intervention, 78
- METTL14, 152–153
- METTL3, 152–153
- MF. *See* Mycosis fungoides
- MGUS. *See* Monoclonal gammopathy of undetermined significance
- Minimal residual disease (MRD), 364, 396
- MIR223*, 341
- MKL1*, 153–154, 328
- MLL*, 303
- MLL1*. *See* *KMT2A*
- MLL2*, 377
- MLLT10*, 342
- MM. *See* Multiple myeloma
- Monoclonal B-cell lymphocytosis (MBL), 70, 393–394
- Monoclonal gammopathy of undetermined significance (MGUS), 70–71
- Monomorphic epitheliotropic intestinal T-cell lymphoma (MEITL), 475
- Mouse models  
leukemia stem cell model, 83–84  
mature B-cell malignancies  
B-cell development, 226–227  
Burkitt lymphoma, 232–233  
cellular origins, 227–229  
chronic lymphocytic lymphoma/small lymphocytic lymphoma, 242–243  
diffuse large B-cell lymphoma  
*BCL6* dysregulation, 239  
*FBXO11* deletion, 240  
*Gα13* pathway disruption, 240  
NF-κB signaling activation, 241–242  
*PRDM1/BLIMP1*, 241
- follicular lymphoma  
*BCL2* translocation, 234–235  
histone modification genes, 235–237  
*MEF2B*-activating mutations, 238–239  
overview, 233–234  
*RRAGC* mutations, 238  
*TNFRSF14* loss, 237–238
- mantle cell lymphoma, 229–232  
overview, 225–226  
prospects for study, 243–244
- myeloid malignancies  
cohesins, 214  
constitutive versus conditional models, 203–204  
CRISPR–Cas9, 204–205  
epigenetic regulator models
- DNA methylation pathways, 209–212  
histone modification pathways, 212–213
- knock-in models, 203
- overview, 199–202
- somatic mutation studies  
*NPM1*, 205–207  
signaling pathways, 207–209
- spliceosome gene models, 213–214
- TP53, 214–216
- transgenic models, 201
- transplantation models, 204
- myeloproliferative neoplasms  
*ASXL1* mutations, 280–281  
*DNMT3A* mutations, 280  
*EZH2* mutations, 281  
*LNK* mutations, 284  
*NFE2* mutations, 286  
*PPM1D* mutations, 287  
*PTPN11*, 285  
*RUNX1* mutations, 285–286  
*SF3B1* mutations, 283–284  
*SRSF2* mutations, 282  
*TET2* mutations, 279  
*TPE53* mutations, 287  
*U2AF1* mutations, 283  
*ZRSR2* mutations, 283
- MPAL*, 374
- MPL*, 257, 276, 326
- MPL*, 272
- MPNs. *See* Myeloproliferative neoplasms
- MPP. *See* Multipotent progenitor
- MRD. *See* Minimal residual disease
- MSI1*, 158–159
- MSI2*, 158–159, 162, 164
- MTHFD2*, 183
- Multiple myeloma (MM)  
cancer cell biology targeting, 492–493  
clonal hematopoiesis, 71, 76  
immunological targeting, 493–497  
novel therapies  
classification of therapies, 488–489  
incorporation into combination therapies, 489–490  
plasma cell biology targeting, 490–492  
overview, 487–488  
prospects for treatment, 497
- Multipotent progenitor (MPP)  
lineage bias and reprogramming during emergency hematopoiesis, 8  
progeny, 3
- Mxl*, 209
- MYB*, 263
- MYB*, 152–153, 161, 336, 343
- MYBBP1A*, 164

## Index

- MYC, 152, 154–155, 159, 176, 178, 184–185, 187  
MYC, 52, 54, 153, 162, 232–233, 336, 342–343, 448, 452, 492  
Mycosis fungoides (MF), genetics, 56–57, 476  
*MYD88*, 53, 239, 242, 389, 451–453  
Myeloproliferative neoplasms (MPNs)  
    *ASXL1* mutations, 280–281  
    *CBL* mutations, 284–285  
    common mutations, 273–275  
    *DNMT3A* mutations, 279–280  
    *EZH2* mutations, 281  
    *IDH1/2* mutations, 279  
    JAK-STAT signaling pathway mutations, 272, 276  
    *KRAS* mutations, 285  
    *LNK* mutations, 284  
    *NFE2* mutations, 286  
    *NRAS* mutations, 285  
    overview, 271–272  
    *PPM1D* mutations, 287  
    prospects for study, 289  
    *RUNX1* mutations, 285–286  
    *SF3B1* mutations, 283–284  
    *SRSF2* mutations, 282  
    *TET2* mutations  
        clinical studies, 277–279  
        mouse models, 279  
        overview, 276–277  
    therapy, 287–288  
    *TPE53* mutations, 286–287  
    *U2AF1* mutations, 282–283  
    *ZRSR2* mutations, 283  
*MYH11*, 296–297  
germinal center B-cell-derived lymphomas, 451–452  
heterogeneity, 460–461  
immunodeficiency-related lymphoma, 453–454  
lymphomagenesis, 448  
models, 458–460  
overview, 447–448  
post-germinal center and marginal zone  
    B-cell-derived lymphomas, 452–453  
pre-germinal center B-cell-derived  
    lymphomas, 451  
primary cutaneous B-cell lymphoma, 453  
treatment  
    chemotherapy, 455–456  
    immunotherapy, 458  
    overview, 454–455  
    targeted therapy, 456–458  
*NOTCH1*, 176, 337–340, 343, 396, 400, 474  
*NOTCH1*, 50, 162, 242, 389, 451  
*NOTCH2*, 243  
*NOTCH2*, 51, 53  
*NOXA*, 186  
*NPM1*, 74–75, 300–301, 305  
*NR3C1*, 377  
*NRAS*, 205, 207, 285, 303, 336, 364, 439  
*NRF1*, 6  
*NT5C2*, 183  
*NTRK1*, 432, 435  
*NUP214*, 299, 342  
*NUP98*  
*Nup98*, 206  
*NUTM1*, 374

## N

- Natural killer/T-cell lymphoma (NKTCL)  
    clinical presentation, 474  
    pathogenesis, 474–475  
*NCOA2*, 432  
*NFI*, 303–304, 347, 439, 471  
*NF2*, 439  
*NFE2*, 286  
*NF-κB*, 236, 241–242  
NHL. *See* Non-Hodgkin lymphoma  
Nivolumab, 480  
*NKKX2.1*, 336–337, 342  
*NKKX2.2*, 336, 342  
*NKKX2.5*, 336, 342  
NKTCL. *See* Natural killer/T-cell lymphoma  
*Nkx2.3*, 206  
*NKX3.1*, 341  
Non-Hodgkin lymphoma (NHL)  
    epidemiology, 35–38  
    genetics, 450–451

## O

- OGDH*, 180  
Oxidative phosphorylation. *See* Metabolism,  
leukemia/lymphoma  
Oxidative stress  
    hematopoietic stem cell DNA damage and  
        functional decline, 5–6  
    leukemia, 183  
    lymphoma, 187

## P

- P16*, 340  
p38 MAPK, 5–6  
Panobinostat, 488  
*PAR1*, 368  
*PAX5*, 178, 235  
*PAX5*, 364, 368, 372, 375  
*PBX1*, 368  
*PCYT1A*, 187  
PD-1, 479–480

- PDGFRA*, 369  
*PDGFRB*, 369  
*PDH*, 180  
*PD-L1*, 474  
*PDL1*, 55  
*PDL2*, 55  
Pembrolizumab, 480  
Peripheral T-cell lymphoma (PTCL)  
    not otherwise specified, 471–472  
    overview, 154, 467  
*PHF6*, 336, 345  
*PI3K*, 403, 431  
*PICALM*, 342  
*PIGA*, 74  
*PIK3CA*, 372, 431  
*PIK3CD*, 431  
*PIM1*, 52, 452  
*PLCG1*, 56, 476  
PMBL. *See* Primary mediastinal large B-cell lymphoma  
Pomalidomide, 488  
*POT1*, 389  
*PP2A*, 187  
*PPM1D*, 11  
*PPM1D*, 70, 76, 287  
Pralatrexate, 477–478  
*PRC1*, 280, 306  
*PRC2*, 120, 132, 281, 306  
*PRDM1*, 130, 237, 239, 241  
PRIMA-1, 308  
Primary cutaneous B-cell lymphoma (CBCL), 453  
Primary mediastinal large B-cell lymphoma  
    (PMBL), genetics, 55  
*PRPF40B*, 282  
*PRPF8*, 307  
*PSEN1*, 339  
PTCL. *See* Peripheral T-cell lymphoma  
*PTD*, 299  
*PTEN*, 152, 178, 181  
*PTEN*, 339, 346  
*PTPMT1*, 6  
*PTPN11*, 285, 303, 364  
*PU.1*, 8, 343  
PUMA, 186
- R**
- RAD21*, 121, 214, 329  
*RAD21*, 307  
RAF, isoforms, 430–431  
*RAF1*, 425, 439  
RAS, isoforms, 178, 431  
*RB1*, 328, 340, 364  
*RBM15*, 152–154, 328  
*RBM39*, 151–152, 160–161, 164  
*RBPs*. *See* RNA-binding proteins  
*RDD*. *See* Rosai–Dorfman–Destombes disease  
*RELA*, 241  
*RELB*, 241  
*RET*, 435  
*RHOA*, 470–471, 474, 476  
Richter's transformation. *See* Chronic lymphocytic leukemia  
Rituximab, 398, 455–456  
*RLTPR*, 476  
RNA-binding proteins (RBPs). *See also specific proteins*  
    noncoding RNA regulators in leukemia/lymphoma  
        *LIN28A*, 154–155  
        *LIN28B*, 154–155  
        *MYC*, 152  
    overview in leukemia/lymphoma, 145–150  
    RNA modifier regulators in leukemia/lymphoma  
        *METTL3*, 152–153  
        *RBM15*, 153–154  
    RNA stability and translation regulators in leukemia/lymphoma  
        *EIF4e*, 155–157  
        *hnRNPk*, 159–160  
        *HuR*, 155–156  
        insulin-like growth factor binding proteins, 157–158  
        *MSI2*, 158–159  
        *SYNCRIP*, 159  
    splicing regulators in leukemia/lymphoma  
        *RBM39*, 151–152  
        *SF3B1*, 150–151  
        *SRSF2*, 150–151  
        *U2AF1*, 150–151  
    therapeutic targeting in leukemia/lymphoma  
        cap-dependent translation, 161–162  
        *LIN28*, 161  
        *MSI2*, 162  
        prospects, 162–164  
        *RBM39*, 160–161  
        spliceosome, 160  
*ROR-1*, 392  
*RORA*, 263  
Rosai–Dorfman–Destombes disease (RDD)  
    cellular origins, 432–433  
    clinical presentation, 430  
    immunophenotypic features, 429  
    treatment, 433–435  
*RPL10*, 348  
*RRAGC*, 234, 238  
*RUN2*, 336  
*RUNX1*, 264, 282  
*RUNX1*, 255, 259–260, 262, 285–286, 296–297, 301, 308, 321, 323–325, 344, 367–369  
*RUNX1T1*, 296–297

## Index

- | S   | T   |
|---|---|
| S1PR2, 240                                      | <i>TAF15</i> , 372                                    |
| SAHM1, 340                                      | <i>TAL1</i> , 336, 341, 343                           |
| SALL1, 374                                      | <i>TAL2</i> , 341                                     |
| SCD1, 182                                       | T-ALL. <i>See</i> T-cell acute lymphoblastic leukemia |
| SEH2B, 242                                      | <i>Tax</i> , 473                                      |
| SESTRIN1, 186                                   | <i>TBX21</i> , 472                                    |
| SET, 342  | T-cell acute lymphoblastic leukemia (T-ALL)           |
| SETD1B, 471                                     | cell cycle disruption, 340–341                        |
| SETD2, 364, 377                                 | epigenetic regulator mutations                        |
| SETD2, 475                                      | <i>EED</i> , 345                                      |
| Sézary syndrome, genetics, 56–57, 476           | <i>EZH2</i> , 345                                     |
| SF1, 282  | <i>KDM6A</i> , 345                                    |
| SF3A1, 282                                      | overview, 344–345                                     |
| SF3B1, 150–151, 160, 282                        | <i>PHF6</i> , 345                                     |
| SF3B1, 242–243, 283–284, 307, 389               | <i>SUZ12</i> , 345                                    |
| SGK1, 452                                       | heterogeneity, 336–337                                |
| SH2B3, 369                                      | NOTCH1  |
| SHMT, 187                                       | activation, 337–338                                   |
| SIRT7, 6  | oncogenetic pathways and effector                     |
| SLAMF7, 494                                     | mechanisms, 338                                       |
| SLC1A3, 183                                     | therapeutic targeting, 338–340                        |
| SMARCA2, 372                                    | overview, 335–336                                     |
| SMARCC1, 476                                    | ribosomal protein mutations, 347–348                  |
| SMC1A, 121, 214                                 | signaling pathway oncogenic activation                |
| SMC3, 121, 214                                  | ABL1 fusion genes, 347                                |
| SMRT, 236                                       | IL7 receptor, 346                                     |
| SMZL. <i>See</i> Splenic marginal zone lymphoma | JAK-STAT, 346–347                                     |
| SNHG5, 348                                      | PI3K-AKT, 346   |
| SOCS1, 55                                       | RAS-MAPK, 347   |
| SOX4, 263                                       | transcription factors                                 |
| SOX11, 50                                       | oncogenes   |
| SOX11, 451                                      | homeobox transcription factors, 342                   |
| SPEN, 452                                       | <i>MYB</i> , 343                                      |
| SPI1, 264                                       | <i>MYC</i> , 342–343                                  |
| SPI1, 336, 343                                  | overview, 341–342                                     |
| Splenic marginal zone lymphoma (SMZL),          | <i>SPI1</i> , 343                                     |
| genetics, 51                                    | tumor suppressor genes                                |
| SREBP1, 187                                     | <i>BCL11B</i> , 344                                   |
| SRSF2, 150–151                                  | <i>ETV6</i> , 343                                     |
| SRSF2, 214, 257, 282, 287, 307, 308             | <i>GATA3</i> , 344                                    |
| STAG1, 121, 307                                 | <i>LEF1</i> , 344                                     |
| STAG2, 121, 214, 307, 329                       | <i>RUNX1</i> , 344                                    |
| STAT3, 159                                      | <i>WT1</i> , 344                                      |
| STAT3, 472, 475–476                             | T-cell lymphoma. <i>See also specific lymphomas</i>   |
| STAT5, 14                                       | classification of mature lymphomas, 468               |
| STAT5B, 56, 347, 475–476                        | treatment of mature lymphomas, 476–480                |
| STMN1, 343                                      | T-cell prolymphocytic leukemia (T-PLL), genetics, 56  |
| SUZ12, 120, 336, 345                            | T-cell receptor (TCR), sequencing, 57–58              |
| SYK, 456  | TCF3, 232   |
| SYNCRIP, 159                                    | TCF3, 54, 368–369                                     |
| SYNCRIP, 348                                    | TCF7, 343   |
|   | TCL1, 243   |

- TCL1A*, 56  
*TCL1B*, 56  
TCR. *See* T-cell receptor  
*TCRA*, 342  
*TCRB*, 343  
*TERT*, 77  
*TET2*, 56, 70, 74–75, 77–78, 117, 119, 121, 128–130, 211–212, 237, 255, 260, 276–279, 305, 469–471, 476  
*TET2*, 7, 11, 13–14, 184  
*TGFB1*, 437  
TIM-3, acute myeloid leukemia therapeutic targeting, 93, 100–101  
*TKD*, 302  
*TLX1*, 336–337, 342–343, 347  
*TLX3*, 336–337, 342–344, 347  
TMD. *See* Transient myeloproliferative disorder  
*TNFAIP3*, 51, 471  
*TNFRSF14*, 52, 234, 237–238  
*TNFRSF17*, 488  
*TNFRSF1B*, 476  
Tofacitinib, 479  
*TP53*, 214–216, 252  
*TP53*, 11, 13, 49–53, 56, 70, 74, 76, 128, 255, 299–300, 319, 364, 375, 451–452, 471  
*TPE53*, 286–287  
*TPEN*, 161  
T-PLL. *See* T-cell prolymphocytic leukemia  
*TRAF3*, 241, 471  
Transient myeloproliferative disorder (TMD)  
    clinical and biological features, 324–325  
    transforming mutation acquisition, 325–326  
*TRIB2*, 341  
*TYK2*, 56
- U**  
*U2AF1*, 150–151, 160, 283  
*U2AF1*, 214, 282–283, 307
- U2AF2*, 282–283  
*U2AF2*, 307  
*UTX*, 213
- V**  
*VAV1*, 471  
Vemurafenib, resistance mechanisms, 439  
Venetoclax, 183  
Vitamin C, clonal hematopoiesis intervention, 77–78  
*VWF*, 8
- W**  
*WHSC1*, 364, 368  
*Wnt*, 13  
*WT1*, 342, 344  
*WTAP*, 152–153
- X**  
*Xfp521*, 206  
*XPO1*, 389
- Y**  
*YAP1*, 374  
*YTHDF2*, 153  
*YTHDF2*, 471
- Z**  
*ZAP70*, 471  
*ZEB1*, 56  
*ZESR2*, 282  
*ZNF362*, 372  
*ZNF374*, 368  
*ZNF384*, 371–372, 374  
*ZNF618*, 374  
*ZRSR2*, 283, 307