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LETTERS TO THE EDITOR

A Resource for Facilitating the Development of Tools in the Education and Implementation of Genomics-Informed Personalized Medicine

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To the Editor: We read with great interest the article, "The Opportunities and Challenges of Implementing Genomics-Informed Personalized Medicine," by Chisholm.[1] The author pointed out that, despite their clinical successes, adoption of some of the clinically proven biomarkers is often limited to major academic medical centers, due partly to a critical barrier in educating health-care providers. To overcome this barrier, apart from employing bioinformatics specialists and developing education materials,[1] a platform is needed for information access using the tools familiar and convenient to health-care providers.

Such tools include the *International Classification of Diseases* (ICD) codes for defining, studying, and managing diseases and treatments,[2] the Systematized Nomenclature of Medicine for clinical documentation and reporting,[3] and the Unified Medical Language System for biomedical terminology.[4] By further linking these tools with biomarkers, in addition to information refinement and presentation-material development, the relevant information may be conveniently accessed via hyperlinks in an e-health (electronic, communication-supported health-care) system. Most biomarkers are molecular based, which presents an educational challenge for those familiar with only the histopathology-based disease-classification systems. Linking ICD codes and biomarkers enables easy cross-links to bioinformatics resources for genomic, structural, pathway-based, and functional information and facilitates research from e-health records.

Moreover, knowledge of biomarkers, targets, and drugs is useful for developing and practicing personalized medicine.[5] Targeted therapeutics is naturally linked to molecular-based and cell-based disease-classification systems (e.g., trastuzumab for HER2+ breast cancer). Some known molecular-based and cell-based disease subtypes have ICD-10 codes, but many are uncoded (see **Table 1** for examples). Information on biomarkers, targets, and drugs may be incorporated into the ICD codes for coding these subclasses and refining patient and drug–response subpopulations to facilitate the diagnosis, prescription, monitoring, and management of personalized medicine.

Although many have yet to be clinically tested, biomarkers are available for the majority of the known molecular-based and cell-based disease subtypes (examples are shown in **Table 1**). However, many more are needed for comprehensive coverage of patient subpopulations. For instance, HER2+ breast cancer needs to be further divided into HER2E-mRNA and luminal-mRNA subgroups based on a 302-gene multimarker set. $BRAF^{V600E}$ metastatic melanoma treated with the $BRAF^{V600E}$ inhibitor dabrafenib frequently develops drug resistance due to drug-escape pathway activation, which requires multiple markers for indicating individual variations of these drug-escape activities.

To support future efforts, we linked the ICD codes to 1,755, 893, and 5,697 literature-reported biomarkers, targets, and drugs, respectively (http://bidd.nus.edu.sg/group/ttd/ttd.asp). All links were manually checked according to disease indications. For biomarkers, the corresponding IDs from all major bioinformatics databases are provided.

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CONFLICT OF INTEREST

The authors declared no conflict of interest.

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Table 1 Examples of diseases and their molecular-based or cell-based subtypes, ICD codes (marked as NA if unavailable), and the availability (A) or unavailability (NA) of the corresponding diagnostic, prognostic, and theragnostic biomarkers

Disease or disease type (ICD-10 code)	Molecular/cell-based subtype (ICD-10 code)	Diagnostic biomarkers	Prognostic biomarkers	Theragnostic biomarkers
Breast cancer (C50.0–50.9)	Basal-like (NA)	A	A (clinical trial)	A (clinical trial)
	Luminal types ER+ (C50.X + Z17.0)	A (clinical use)	A (clinical use)	A (clinical use)
	Luminal A ER+ and low-grade (NA)	A	A	NA
	Luminal B ER+ but often high-grade (NA)	A	A	A
	Luminal ER−/PR+ (NA)	A	A (clinical use)	A (clinical use)
	HER2+	A (clinical use)	A (clinical use)	A (clinical use)
	Claudin-low	A	NA	NA
Lung cancer (34.0–34.9)	NSCLC (NA)	A	A (clinical use)	A (clinical use)
	NSCLC subtype adenocarcinoma (NA)	A	A	A
	NSCLC subtype squamous-cell lung carcinoma (NA)	A	A	NA
	NSCLC subtype large-cell lung carcinoma (NA)	NA	NA	NA
	Small-cell lung carcinoma (NA)	A	A (clinical trial)	NA
Acute lymphoblastic leukemia (C91.0)	Nondistinguished	A (clinical use)	A (clinical use)	A (clinical use)
	Precursor B acute lymphoblastic leukemia (NA)	NA	A	NA
	Precursor T acute lymphoblastic leukemia (NA)	A	NA	NA
	Burkitt's leukemia (C91.A)	A	NA	NA
	Acute biphenotypic leukemia (C95.0)	A	NA	NA
Chronic lymphocytic leukemia (C91.1)	Nondistinguished	A (clinical use)	A	A
	B-cell prolymphocytic leukemia (C91.3)	A	NA	NA
	T-cell prolymphocytic leukemia (C91.6)	A	NA	NA
Acute myelogenous leukemia (C92.6, C92.A)	Nondistinguished	A (clinical use)	A (clinical trial)	A (clinical trial)
	Acute promyelocytic leukemia (C92.4)	NA	A (clinical use)	A (clinical use)
	Acute myeloblastic leukemia (C92.0)	A	A	NA
	Acute megakaryoblastic leukemia (C94.2)	A	NA	NA
Chronic myelogenous leukemia (C92.1)	Nondistinguished	A (clinical use)	A (clinical use)	A (clinical use)
	Chronic monocytic leukemia (C93.1)	NA	A	NA
Large granular lymphocytic leukemia (C91.Z)	Nondistinguished	A	NA	NA
	T-cell large granular lymphocytic leukemia (NA)	A	NA	NA
	NK-cell large granular lymphocytic leukemia (NA)	NA	NA	NA
Other types of leukemia	Adult T-cell leukemia (C91.5)	A	A	NA
	Hairy-cell leukemia (C91.4)	A	A	A

"Clinical use" and "clinical trial" indicate that one or more of the biomarkers in the category are clinically used (or are recommended for clinical use by the US Food and Drug Administration and clinical societies) and in clinical trials, respectively.

ER, estrogen receptor; ICD, *International Classification of Diseases*; NK, natural killer; NSCLC, non–small cell lung carcinoma; PR, progesterone receptor.