

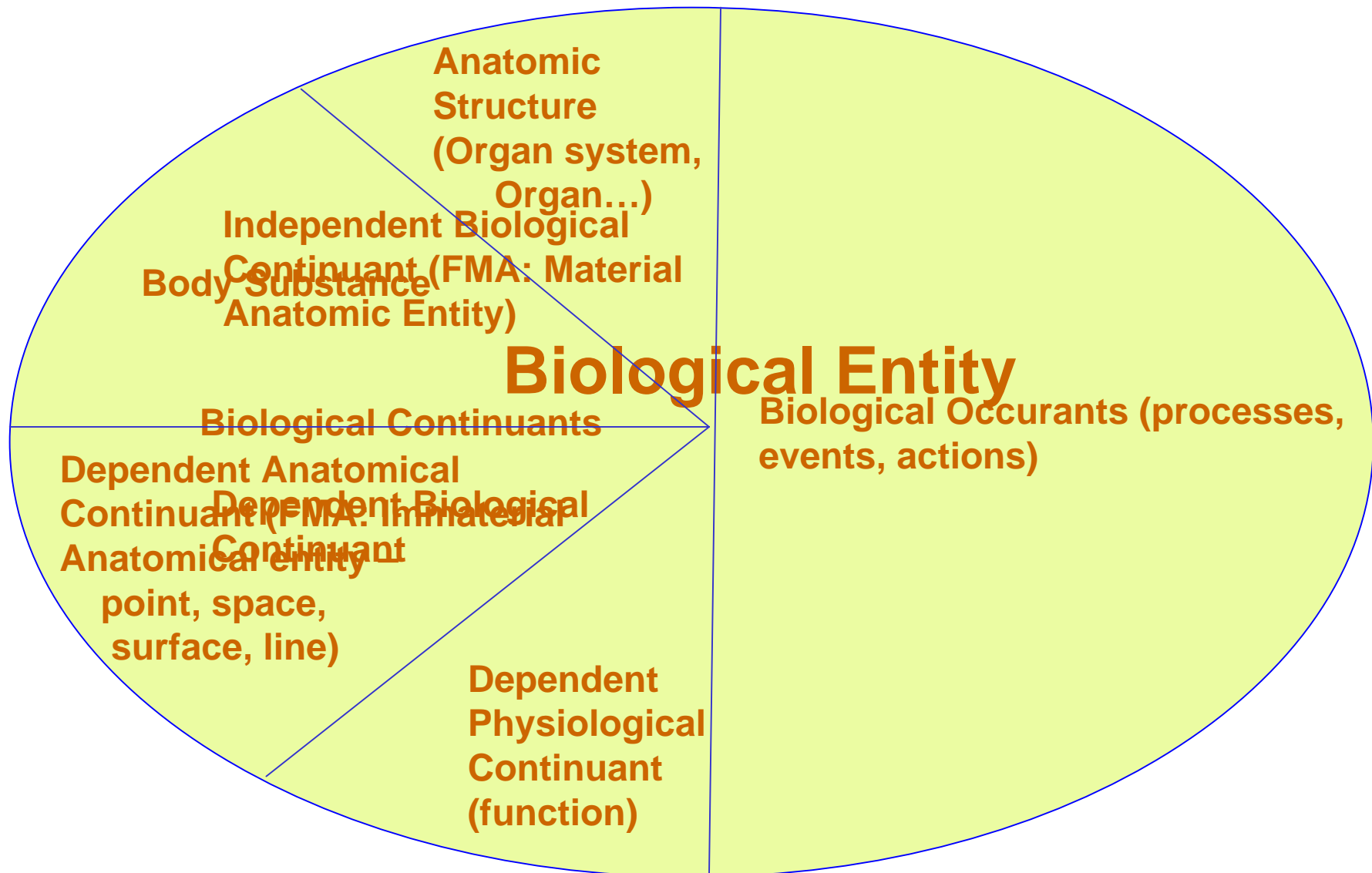
Ontology of Pathological Structures

Mapping the Human Body
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Biological Entity classification using Realism



Tumor, Node, Metastasis (TNM) Classification

CI	TNM definition	Level of Granularity	Other partitions
Tis	Carcinoma in situ: intraepithelial or invasion of the lamina propria	Intraepithelial cell (C); Epithelium & lamina propria (ORP/MPOT)	
T1	Tumor invades submucosa	Submucosa of colon (ORP/MPOT)	
T2	Tumor invades muscularis propria	Muscularis mucosa of colon (ORP/MPOT)	
T3	Tumor invades through the muscularis propria into the subserosa, or into nonperitonealized pericolic or perirectal tissues	Subserosa of colon (ORP/MPOT), nonperitonealized pericolic or perirectal tissues (ORP/MPOT-E)	path of invasion (pathogenesis)
T4	Tumor directly invades other organs or structures, and/or perforates visceral peritoneum	organs (OR-E), visceral peritoneum (ORP)	path of invasion (pathogenesis)
N0	No regional lymph node metastasis	--	
N1	Metastasis in 1 to 3 regional lymph nodes	lymph node (ORP), collection of lymph nodes (ORP-C)	number
N2	Metastasis in 4 or more regional lymph nodes	lymph node (ORP), collection of lymph nodes (ORP-C)	number
M0	No distant metastasis	--	
M1	Distant metastasis	ORG	

Problems with ontologies of Pathological structures

Indescent anatomy:

NCI Thesaurus

Colon part-of Large Intestine

Colon synonym Large Intestine

Snomed CT: *Amputation of leg is-a Amputation of
any part of lower limb, including total amputation*

SCOP classification: *Alfa proteins, Beta proteins,
membranous proteins etc.*

Problems with ontologies of Pathological structures

Unclear distinctions between pathological structure, stage and disease

- a. *T2N1M0 stage of colon carcinoma*
- b. *T2N1M0 stage colon carcinoma structure*
- c. *Colon carcinoma disease with T2N1M0 stage colon carcinoma structure*

Inadequate representation of time

*T2N1M0 stage colon carcinoma structure preceded by
T1N1M0 stage colon carcinoma structure preceded by
T1N0M0 stage colon carcinoma structure preceded by
normal colon*

Problems with ontologies of Pathological structures

Inadequate distinction between instance and classes

*T2N1M0 stage colon carcinoma structure preceded by
T1N1M0 stage colon carcinoma structure?*

or

*T2N1M0 stage colon carcinoma structure preceded by
T2N0M0 stage colon carcinoma structure?*

Confusions over relation between normal and abnormal structures

Colon with carcinoma is a Colon ?

Completely cirrhotic liver is a Liver?

*Mucosa of colon with complete Crohn's disease is a
Mucosa of colon ?*

T2N1M1 colon carcinoma structure

Processes involved

T2: Tumor invades muscularis propria

N1: Metastasis in 1 to 3 lymph nodes

M1: Distant metastasis

Pathological structures

T2N1M1 colon carcinoma pathological structure:

T2 colon carcinoma pathological structure implies

*Portion of colon mucosa carcinoma pathological structure and
Portion of colon submucosa carcinoma pathological structure and
Portion of colon muscularis propria carcinoma structure*

T2N1M1 colon carcinoma structure

*N2 colon carcinoma structure implies
1 lymph node with colon carcinoma metastatic structure or
2 lymph node with colon carcinoma metastatic structure or
3 lymph node with colon carcinoma metastatic structure*

*M1 colon carcinoma structure implies
Lung with colon carcinoma metastatic structure or
Liver with colon carcinoma metastatic structure or*

*T2N1M1 colon carcinoma structure is a Collection of
pathological structures*

T2N1M1 colon carcinoma structure

T2N1M1 colon carcinoma structure
has-member *T2 colon carcinoma structure* and
has-member *N1 colon carcinoma structure* and
has-member *M1 colon carcinoma structure*

T2N1M1 colon carcinoma process:
is constituted by abnormal processes
associated with the carcinoma development

T2N1M1 colon carcinomatous process has-part
T2 colon carcinomatous process and has-part
N1 colon carcinomatous process and has-part
M1 colon carcinomatous process

Instance of T2N1M1 colon carcinoma structure

*inst(T2N1M1 carcinoma structure) implies
mucosal carcinoma structure and
muscularis mucosal carcinoma structure and
3 paracolic lymph nodal metastatic structure and
left upper lung lobe metastatic structure*

*T2N1M1 carcinomatous structure transformation_of
T2N1M0 carcinomatous structure transformation_of
T2N0M0 carcinomatous structure transformation_of
T1N0M0 carcinomatous structure transformation_of
TisN0M0 carcinomatous structure transformation_of
Colon part*

Instance of T2N1M1 colon carcinoma structure

*left upper lung metastatic carcinomatous process preceded-by
distant organ metastasis preceded-by
paracolic lymph nodal carcinomatous process preceded-by
lymph nodal metastasis preceded-by
muscularis proprial carcinomatous process preceded-by
trans-submucosal carcinomatous invasion preceded-by
submucosal carcinomatous process preceded-by
transmucosal carcinomatous invasion preceded-by
mucosal carcinomatous process preceded-by
transcellular carcinomatous process preceded-by
epithelial cellular carcinomatous process*

T2N1M1 colon carcinoma processes: Class level

Process workflow which is always true:

*T4 colon carcinomatous process preceded-by
T3 colon carcinomatous process preceded-by
T2 colon carcinomatous process preceded-by
T1 colon carcinomatous process preceded-by
 T_{is} colon carcinomatous process*

*N2 colon carcinomatous process preceded-by
N1 colon carcinomatous process preceded-by
N0 colon carcinomatous process*

*M1 colon carcinomatous process preceded-by
M0 colon carcinomatous process*

T2N1M1 colon carcinoma processes: Class level

T4N2M1 implies preceded-by (*T3N2M1* or *T4N1M1* or *T4N2M0*)
T3N2M1 implies preceded-by (*T2N2M1* or *T3N1M1* or *T3N2M0*)

.....

$T_x N_y M_z$ implies preceded-by ($T_{x-1} N_y M_z$ or
 $T_x N_{y-1} M_z$ or $T_x N_y M_{z-1}$)
where $4 = x = 1$ and $2 \geq y \geq 0$ and $1 \geq z \geq 0$

Tis colon carcinoma structure can only coexist with
N0 colon carcinoma structure
and *M0 colon carcinoma structure*;
and accordingly the processes

Levels of granularity

Anatomical levels of granularity in human body:

Organism

Organ system / Cardinal body part

Organ

Organ part / Maximum portion of tissue

Cell

Sub-cellular organelle

Molecule

Atom

Fundamentals behind the levels:

Grains, Structure, Origin

Results from database-approach

B I O M E D I C A L O N T O L O G Y

RNA binding	nucleus	30
DNA binding	nucleosome	31
transcriptional activator activity	nucleus	31
structural constituent of ribosome	cytosolic large ribosomal subunit (sensu Eukarya)	32
transmembrane receptor activity	integral to plasma membrane	36
protein binding	cytoplasm	36
zinc ion binding	nucleus	43
protein binding	nucleus	45
receptor activity	integral to plasma membrane	56
G-protein coupled receptor activity	integral to plasma membrane	70
DNA binding	nucleus	100
antigen binding	extracellular	123
transcription factor activity	nucleus	171

Finer levels of granularity

Where are the cells with such abnormalities located?

Not the ulcer

Not the necrotic portion

Not in the blood vessels, lymphatic vessels which
feed into colon carcinoma structure

Such abnormalities exist within the living cancerous cells

Mucosal ulcer implies not (*portion of mucosa*) and
ulcer margin and *ulcer shape* and ...

Finer levels of granularity

*Colon with T2N1M1 carcinoma and necrotic mucosal ulcer implies
.... and not (portion of colon mucosa)
and necrotic tissue derived from portion of colon mucosa
and cancerous portion of colon mucosa*

absent portion of colon mucosa is like unicorn
Not a universal

Characteristics of cancerous cells do not exist in the
Absent portion of mucosa as there are no mucosal cells there

Characteristics of cancerous cells do not exist in the
normal portion of mucosa as there are no cancerous cells there

Finer levels of granularity

Abnormalities which are represented in
Gene Ontology Annotations,
Pathways/Portions/Quantitative representations
active in carcinomas in Reactome,
Protein-protein interactions present in IntAct, DIP, BIND for
such pathways
are NOT located in complete portion of mucosa

*Colon with T2N1M1 colon carcinoma structure and
necrotic mucosal ulcer is-a Colon*
LHS entity does not have all cells / all portions of tissue /
organ parts which RHS entity has
LHS entity has some more cells / portions of tissue /
“organ” parts which RHS entity has

Ontology of pathological structures

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