# Meeting notes HP MP

29th of October , Berlin

# Precondition

Current documentation about design patterns is a bit too complicated at the moment. (https://docs.google.com/document/d/1LOYQ6pOlvapzJhHbSA_Rb3aZYylXZ564B78jiysvB-U/edit#) There is also this google sheet with more specific examples: https://docs.google.com/spreadsheets/d/1JTe0l_HNyuBU4JalUdZKijzfu3osL7BmiqWC6Hcb2Mg/edit#gid=0
Problems in current documentation:

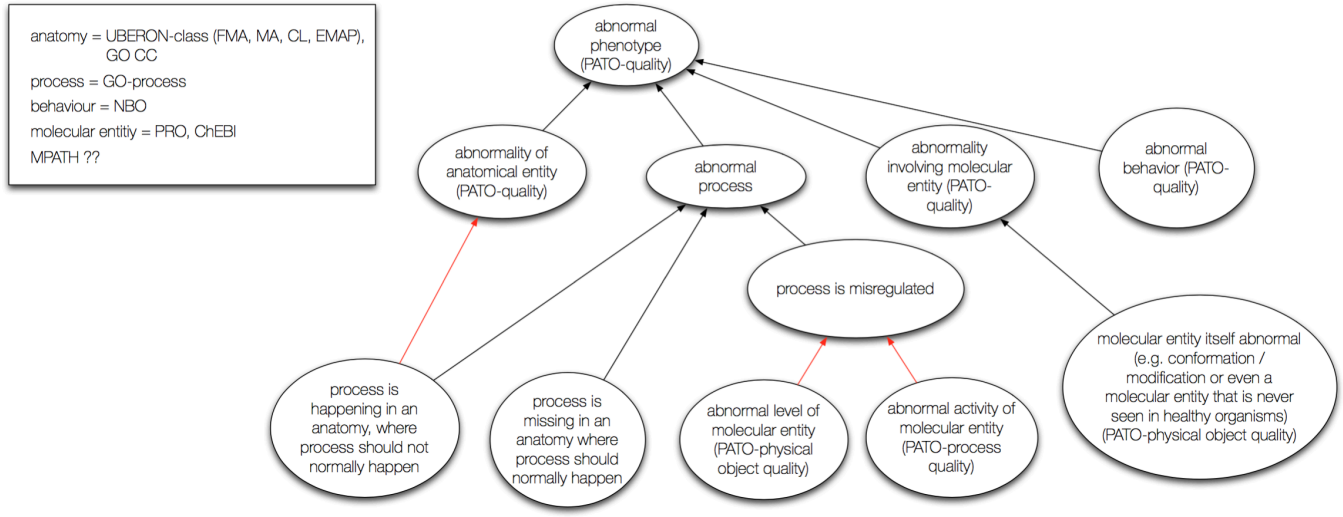
- Contains duplicated examples/templates for one pattern.
- In general the document mixes:
    - Patterns
    - Templates
    - Concepts
    - Examples
- Not optimal structure

# Novel representation

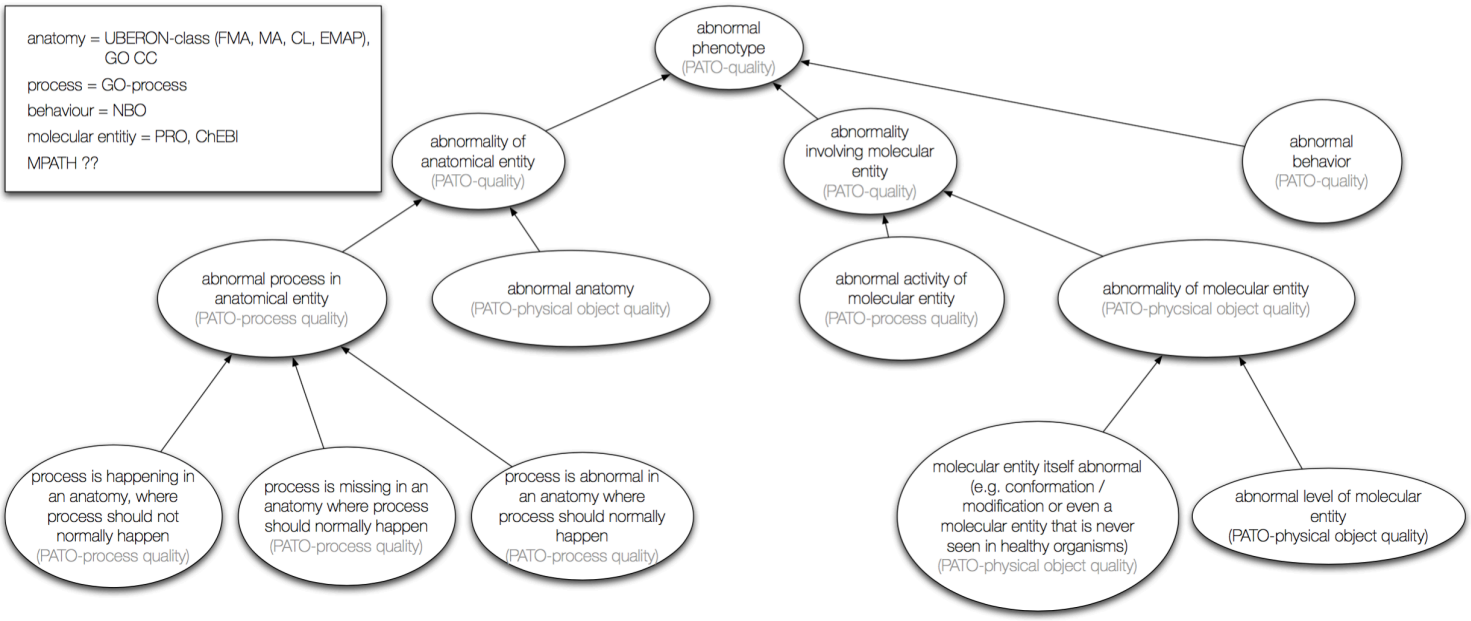
At first we want to make a distinction between **patterns**, **templates,** and **phenotype classes**.
A **pattern** is something like “an abnormal process”, i.e. a very general kind of phenotypic abnormality.
A **template** is a specific kind of pattern ; these are recurring instances of types of phenotypes (e.g. ossification/pigmentation/size of some anatomy) for which we define here **one (!) template**. (i.e. we define if we have to use ossification in GO or PATO:ossified)
The **phenotype classes** are the classes from HP, MP, ZP, etc. and each of theses classes should belong to exactly one template.

The first idea is to describe the **patterns** in a semi-formal schema (conceptualisation). In this schema every pattern is represented as a circle and they are connected by directed edges. An edge between pattern A and B, stands for something like “*A phenotype class that belongs to pattern A can be a subclass of a phenotype class that belongs to pattern B”.*

We found that there are actually only a small number of (general) **patterns** that are found in the phenotype ontologies.




*The red edges correspond to cases where we currently do not have enough expressivity. E.g. we do not have a pattern for something like ‘occurs_in_part_of’ (see below). Also we miss the axioms that connect molecular entities with the GO processes that regulate them (level, activity, etc.). The question mark denotes the fact that we are not sure if we want to have this inference at all (example astrocytosis). This was the first version and we think the next figure would be a better representation. (This will require changing HP/MP)*




*Revised version of the patterns and their relations. At the moment we think this would be the way to go, but this will require several changes in the ontologies.*

## Processes as states

We suggest to get rid of many GO processes in the phenotype ontologies. We think that in 95% of the cases it is not *the process* that is observed/measured, but the *state that results* from the process being abnormal. Thus, we think it is better to *replace*

- Proliferation with PATO:increased number of X
- Degeneration with use PATO:degenerate
- ...

If it is really the process that is abnormal, we suggest that each process has to inhere in some anatomy, i.e. there can be no general *abnormality of P,* but it has to be an *abnormality of P (‘part of’ some A)*

*From process to anatomy (i.e. missing GO axioms):*
If we do not follow the above suggestion, we have to bridge GO:process with CL/UBERON using a proper relation (*has input*? Chris’ ideas?).
E.g. “Defective B cell activation” uses GO:*B cell activation* and could potentially be inferred as “Abnormality of B cell physiology”, but we are missing an axiom similar to the GO-axiom “B cell activation” has input some “B cell”. How to achieve that?

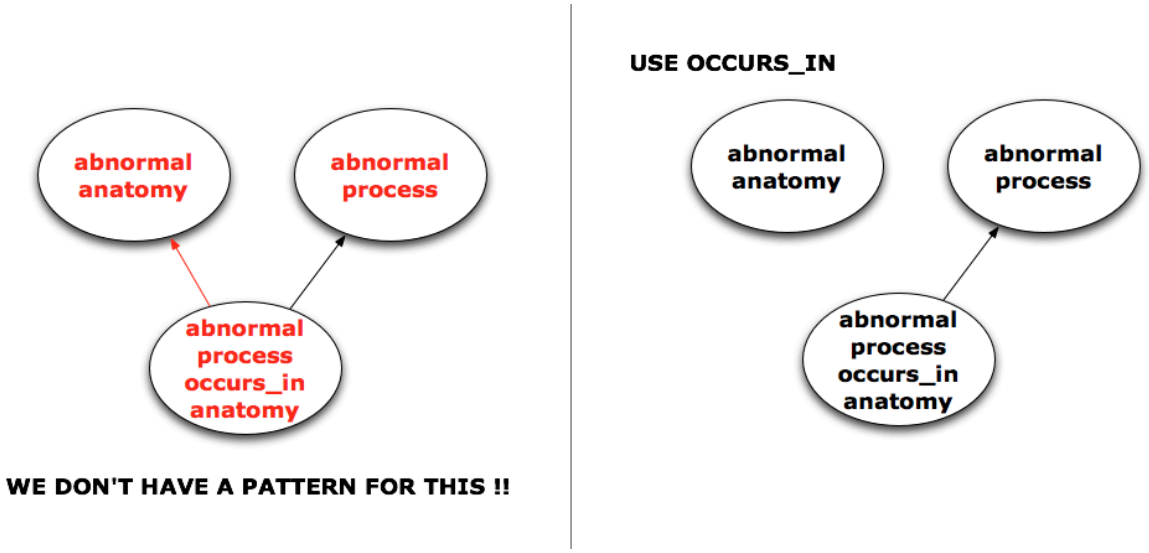
If we do replace the processes with states, we will have problems such as this:
Instead of abnormal GO:*ossification*, we would use abnormal PATO:*density*. But we still would like to infer at some point, that abnormal PATO:*density* is probably caused by abnormal GO:*ossification*. What would be the best way to achieve this?

## Pathology

A problem that is currently not solved is **pathology**. We are not sure what pathology really is. Is it a process, a morphology, a quality,  … ? This has to be discussed:
For example, we are unsure if we should use processes or morphology (e.g. sclerosis (MPATH-process) vs. sclerotic (PATO)
Further ideas: ossified, sclerotic, fibrotic , pigmented, localised, to add to PATO

## Missing pattern ?

This is related to the question mark arrow in Figure 1. That means, if we want to link HP:*Astrocytosis* with both “abnormal GO:*cell proliferation*” AND “HP:abnormality of astrocytes”, we don’t have a pattern for this. But we think we don’t want this inference anyway. Can/Should we infer that a process P is in abnormality of A, because we know that P occurs in A ? Example: coagulation!
See figure below:



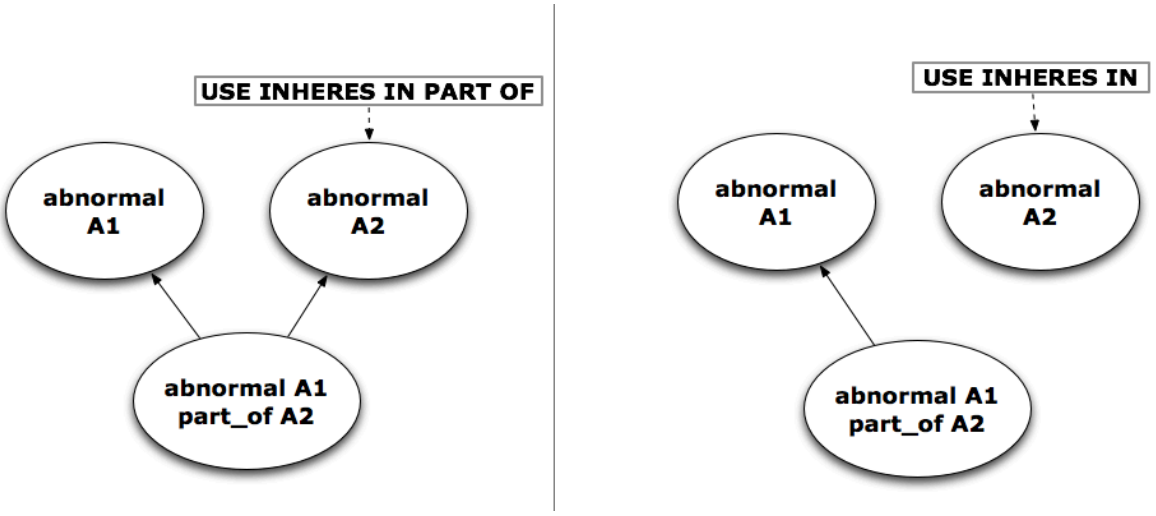
# Patterns

For each node in the figure there should be a owl-class axiom in manchester syntax.

## Abnormal A

```
'has part' some
      (‘physical object quality’ and
      ('inheres in (part of)' some [A])
      and ('has modifier' some abnormal))
```

- A can also be : ([A1] and (‘part of’ some [A2])))
- ‘inheres in’ can also be ‘inheres in part of’




## Abnormal P

```
'has part' some
      ([PATO:process quality] and
      ('inheres in' some ([GO process] and (‘part of’ some [UBERON
      or GO:CC])
      and ('has modifier' some abnormal))
```

Every P has to be restricted to some A.

## P is abnormal (PATO:process quality) in some A

same as above!

An abnormality in a process may be further described in separate cases for modeling:

## P is happening in some A, where P should not normally happen

**DO WE STILL NEED THIS CASE IF WE MODEL THE END POINT**
** consider apoptosis case, other cases where a GO specific term will not exist (gliosis? astrocytosis?) Or should all be the anatomy end point?

```
'has part' some
       (‘having extra processual parts’ and
       ('inheres in' some ([GO process]
                  and ‘occurs in’ some [UBERON or GO:CC]))
       and ('has modifier' some abnormal))
```

## P is missing in some A, where P should in normally happen

```
'has part' some
 (‘    ’ and
 ('inheres in' some ([GO process]
             and ‘occurs in’ some [UBERON or GO:CC]))
 and ('has modifier' some abnormal)
```

** consider apoptosis case - when GO specific term for anatomy exists and when it does not (do we model or request the GO term?)

# Abnormality involving ME

```
'has part' some
 (‘quality’ and
 ('inheres in (part of)' some [ME])
 and ('has modifier' some abnormal))
```

### Abnormality of ME

```
'has part' some
       (‘physical object quality’ and
       ('inheres in part of' some [ME])
       and ('has modifier' some abnormal))
```

### Abnormal level of ME

```
'has part' some
     (‘amount’ and
     ('inheres in (part of)' some [ME])
     and ('has modifier' some abnormal))
```

### ME itself is abnormal (modified) and this modified ME is never seen in healthy individuals

```
'has part' some
      (‘molecular quality’ and
      ('inheres in' some [ME])
      and ('has modifier' some abnormal))
```

### Abnormal activity of ME

```
'has part' some
      (qualitative and
      ('inheres in part of' some [GO molecular function])
      and ('has modifier' some abnormal))
```

*N+ote: A GO term is used to describe the activity of a ME. We have an issue here of how to relate to the molecular entity itself. For example, ‘abnormal aldehyde oxidase activity’ [MP:0020026] could be related to ‘aldehyde oxidase’ [PR_000004089], or GO has other relations to reactions RHEA:16832 and MetaCyc:ALDEHYDE-OXIDASE-RXN,EC:1.2.3.1. This is similar concept to the GO processes example above ‘B cell activation’ where we need to bridge to the UBERON B cell term? Here we would need to bridge the GO molecular function term to ChEBI or PRO.*

*If GO molecular function term does not exist it should be requested.*

## Abnormal behavior

```
'has part' some
      (quality and
```

```
('inheres in' some [NBO])
and ('has modifier' some abnormal))
```

# Templates

## Abnormal anatomy (A)

### abnormal morphology of A

'has part' some
	(morphology
	and ('inheres in' some [A])
	and ('has modifier' some abnormal))

'has part' some
	(morphology
	and ('inheres in' some [A1] and ‘part of’ some [A2]])
	and ('has modifier' some abnormal))

MP phenotype class examples:
‘abnormal heart morphology’ [MP:0000266]
'has part' some
	(morphology
	and ('inheres in' some heart)
	and ('has modifier' some abnormal))

‘abnormal mitochondrion morphology’ [MP:0006035]
'has part' some
	(morphology
	and ('inheres in' some mitochondrion)
	and ('has modifier' some abnormal))

‘abnormal cardiomyocyte mitochondrion morphology’ [MP:xxxx]
'has part' some
	(morphology
	and ('inheres in' some (mitochondrion and ‘part of’ some cardiomyocyte)))
	and ('has modifier' some abnormal))

### absent A

'has part' some
	(absent

and ('inheres in' some [A])
and ('has modifier' some abnormal))

MP example:
‘absent heart’
'has part' some
(absent
and ('inheres in' some heart)
and ('has modifier' some abnormal))

## abnormal, in/decreased A  size

abnormal A size
'has part' some
(size and ('inheres in' some [A]) and ('has modifier' some abnormal))

'has part' some
(‘decreased size’ and ('inheres in' some [A]) and ('has modifier' some abnormal))

'has part' some
(‘increased size’ and ('inheres in' some [A]) and ('has modifier' some abnormal))

## abnormal, in/decreased A  number

'has part' some
(amount and ('inheres in' some [A]) and ('has modifier' some abnormal))

'has part' some
(‘decreased amount’ and ('inheres in' some [UBERON or GO CC]) and ('has modifier' some abnormal))

'has part' some
(‘increased amount’ and ('inheres in' some [UBERON or GO CC]) and ('has modifier' some abnormal))

## abnormal, in/decreased A  weight

'has part' some
(weight and ('inheres in' some [UBERON or GO CC]) and ('has modifier' some abnormal))

'has part' some
(‘decreased weight’ and ('inheres in' some [UBERON or GO CC]) and ('has modifier' some abnormal))

'has part' some
(‘increased weight’ and ('inheres in' some [UBERON or GO CC]) and ('has modifier' some abnormal))

## calcified A

'has part' some
(calcified and ('inheres in' some [UBERON or GO CC]) and ('has modifier' some abnormal))

MP example:

calcified aorta [MP:0010522]
'has part' some
(calcified and ('inheres in' some aorta) and ('has modifier' some abnormal))

fibrotic A (?) need fibrotic added to pato

## sclerotic A

(?) need sclerotic added to pato

## degenerate A

'has part' some
(degenerate and ('inheres in' some [UBERON or GO CC])
and ('has modifier' some abnormal))

MP example:
ameloblast degeneration [MP:0000129]
'has part' some
(degenerate and ('inheres in' some ameloblast)
and ('has modifier' some abnormal))

# Abnormal Process (P) in some anatomy (A)

'has part' some
(‘process quality’ and
('inheres in' some [GO process])
and ('has modifier' some abnormal))

MP example:
abnormal cell-mediated immunity [MP:0002421]
'has part' some
(quality and ('inheres in' some 'leukocyte mediated immunity') and ('has modifier' some abnormal))

## P is happening in an A, where process should not normally happen

'has part' some
(‘having extra processual parts’ and
('inheres in' some ([GO process] and ‘occurs in’ some [UBERON or GO CC]))
and ('has modifier' some abnormal))

MP example:

astrocytosis [MP:0003354]
currently:

'has part' some
(‘having extra processual parts’ and
('inheres in' some (‘cell proliferation’ and ‘occurs in’ some astrocyte))
and ('has modifier' some abnormal))

'has part' some
(‘having extra processual parts’ and
('inheres in' some (‘cell growth’ and ‘occurs in’ some astrocyte))
and ('has modifier' some abnormal))

perhaps should be defined as end point:

'has part' some
(‘increased number’ and
'inheres in' some astrocyte)
and ('has modifier' some abnormal)

## P missing

'has part' some
(‘lacking procesual parts’ and
('inheres in' some ([GO process])
and ('has modifier' some abnormal))
-Q: we chose ‘lacks processual parts’ over ‘absent’

MP examples:
1) absent cumulus expansion [MP:0009374]

current:
'has part' some
(absent and ('inheres in' some 'ovarian cumulus expansion')
and ('has modifier' some abnormal))

proposed:
'has part' some
(‘lacking processual parts’ and ('inheres in' some 'ovarian cumulus expansion')
and ('has modifier' some abnormal))

2) failure of atrioventricular cushion closure [MP:0000299]

'has part' some
('lacking processual parts' and ('inheres in' some 'endocardial cushion fusion') and ('has modifier' some abnormal))

## P dysregulated

'has part' some
([physical quality of a process] and
('inheres in' some [GO process]
and ('has modifier' some abnormal))

delayed heart looping [MP:0009328]

'has part' some
(delayed and ('inheres in' some 'heart looping')
and ('has modifier' some abnormal))

## Abnormal molecular entity (ME)

```
'has part' some
 (‘quality’ and
 ('inheres in (part of)' some [ME])
 and ('has modifier' some abnormal))

absent ME:
'has part' some
 (absent and
 ('inheres in part of' some [ME])
 and ('has modifier' some abnormal))

MP example:
absent galactosylceramidase [MP:0020266]
'has part' some
 (absent and
 ('inheres in part of' some galactocerebrosidase)
 and ('has modifier' some abnormal))

absent ME in A:
'has part' some
  (absent and
('inheres in part of' some
   (ME and ('part of' some A)))
  and ('has modifier' some abnormal))

  MP example: absent circulating adrenaline [MP:0001742]
'has part' some
  (absent and
('inheres in' some
   (adrenaline and ('part of' some blood)))
  and ('has modifier' some abnormal))
```

## Abnormality of ME

```
'has part' some
 (‘physical object quality’ and
 ('inheres in part of' some [ME])
 and ('has modifier' some abnormal))
```

## Abnormal level of ME

```
 'has part' some
 (‘amount’ and
 ('inheres in (part of)' some [ME])
 and ('has modifier' some abnormal))

abnormal adrenaline level [MP:0003962]
'has part' some
 (amount
 and ('inheres in' some adrenaline)
 and ('has modifier' some abnormal))

 increased/decreased level of ME
 'has part' some
 (‘increased amount’ and
 ('inheres in (part of)' some [ME])
 and ('has modifier' some abnormal))

increased adrenaline level [MP:0003962]
'has part' some
 (‘increased amount’
 and ('inheres in' some adrenaline)
 and ('has modifier' some abnormal))

 'has part' some
 (‘decreased amount’ and
 ('inheres in (part of)' some [ME])
 and ('has modifier' some abnormal))

abnormal level of ME in X location
'has part' some
 (amount and ('inheres in' some
  (ME and
 ('part of' some A)))
 and ('has modifier' some abnormal))

MP example: abnormal circulating adrenaline level [MP:0005660]
'has part' some
 (amount and ('inheres in' some
  (adrenaline and
 ('part of' some blood)))
 and ('has modifier' some abnormal))
```

```
 increased/decreased level of ME in x location

'has part' some
 (‘increased amount’ and ('inheres in' some
  (ME and
 ('part of' some A)))
 and ('has modifier' some abnormal))

MP example: increased circulating adrenaline level [MP:0005660]
'has part' some
 (‘increased amount’ and ('inheres in' some
  (adrenaline and
 ('part of' some blood)))
 and ('has modifier' some abnormal))

'has part' some
 (‘decreased amount’ and ('inheres in' some
  (ME and
 ('part of' some A)))
 and ('has modifier' some abnormal))

MP example: decreased circulating adrenaline level [MP:0005661]
'has part' some
 (‘decreased amount’ and ('inheres in' some
  (adrenaline and
 ('part of' some blood)))
 and ('has modifier' some abnormal))
```

ME itself is abnormal (modified) and this modified ME is never seen in healthy individuals

```
 'has part' some
(‘molecular quality’ and
('inheres in' some [ME])
and ('has modifier' some abnormal))
```

Abnormal activity of ME

```
 'has part' some
(‘process quality’ and
('inheres in part of' some [GO molecular function])
and ('has modifier' some abnormal))

abnormal activity:
abnormal glutamate decarboxylase activity [MP:0012594]
'has part' some
 (quality
```

```
 and ('inheres in' some 'glutamate decarboxylase activity')
 and ('has modifier' some abnormal))

increased activity:
 'has part' some
 (‘increased rate’ and
 ('inheres in part of' some [GO molecular function])
 and ('has modifier' some abnormal))

increased glutamate decarboxylase activity [MP:0012596]
'has part' some
 (‘increased rate’
 and ('inheres in' some 'glutamate decarboxylase activity')
 and ('has modifier' some abnormal))

decreased activity:
 'has part' some
 (‘decreased rate’ and
 ('inheres in part of' some [GO molecular function])
 and ('has modifier' some abnormal))

decreased glutamate decarboxylase activity [MP:0012595]
'has part' some
 (‘decreased rate’
 and ('inheres in' some 'glutamate decarboxylase activity')
 and ('has modifier' some abnormal))
```

## Abnormal behavior

```
 'has part' some
 (qualitative and
 ('inheres in' some [NBO])
 and ('has modifier' some abnormal))

 impaired behavior?
 'has part' some
 (quality and
 ('inheres in' some [NBO])
 and ('has modifier' some abnormal))

 enhanced behavior?
```

```
'has part' some
(quality and
('inheres in' some [NBO])
and ('has modifier' some abnormal))
```

? tumor
increased amount - tumor term