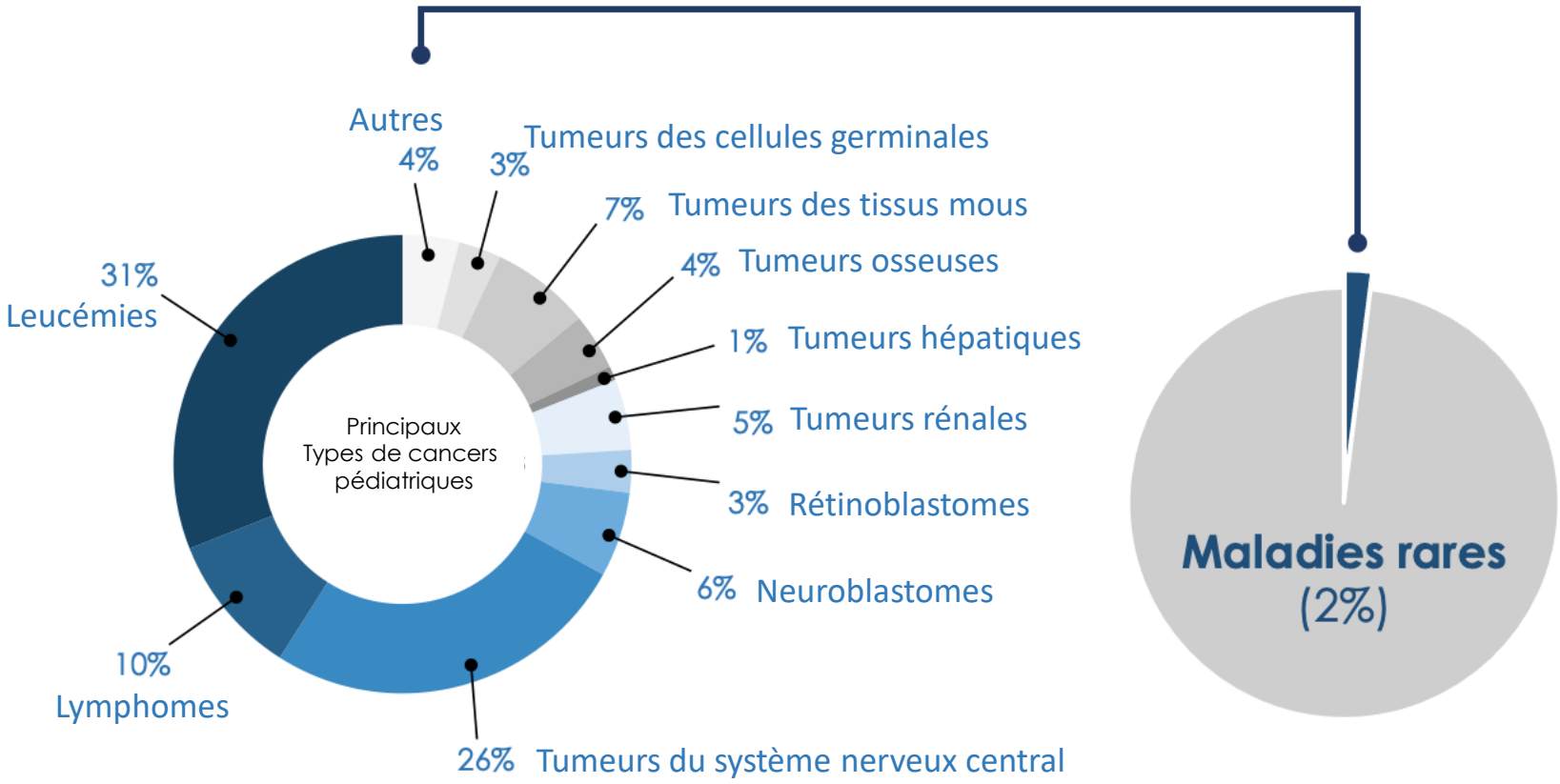
Apport des nouvelles technologies à la recherche fondamentale et translationnelle

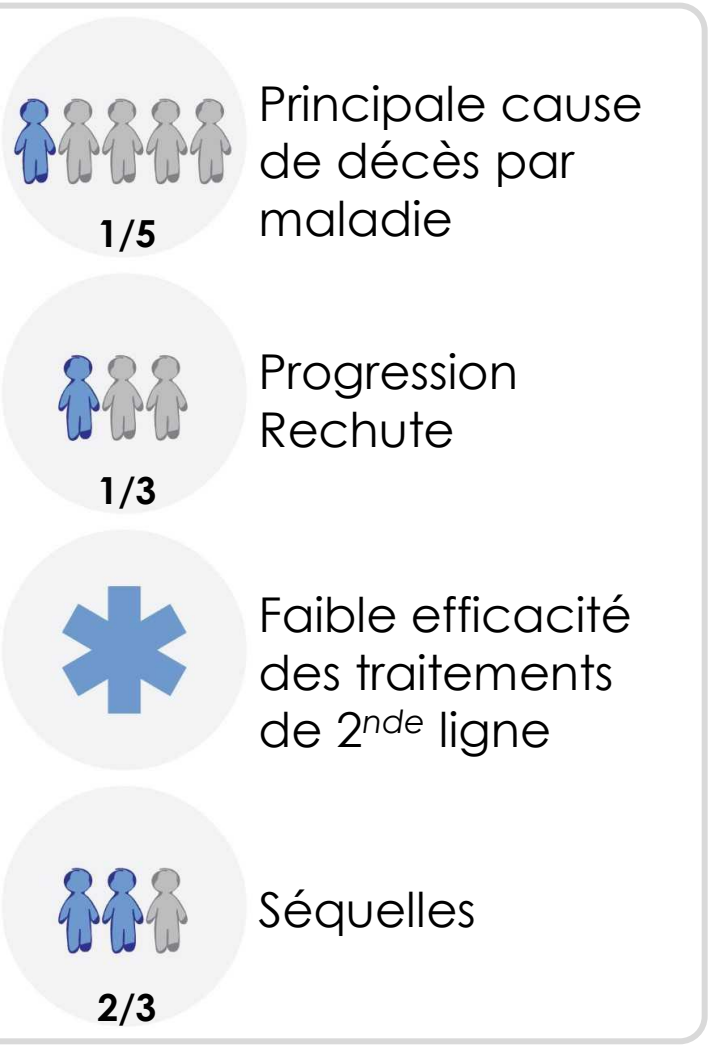
Ex. du réseau national de recherche en oncopédiatrie React4Kids !

REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

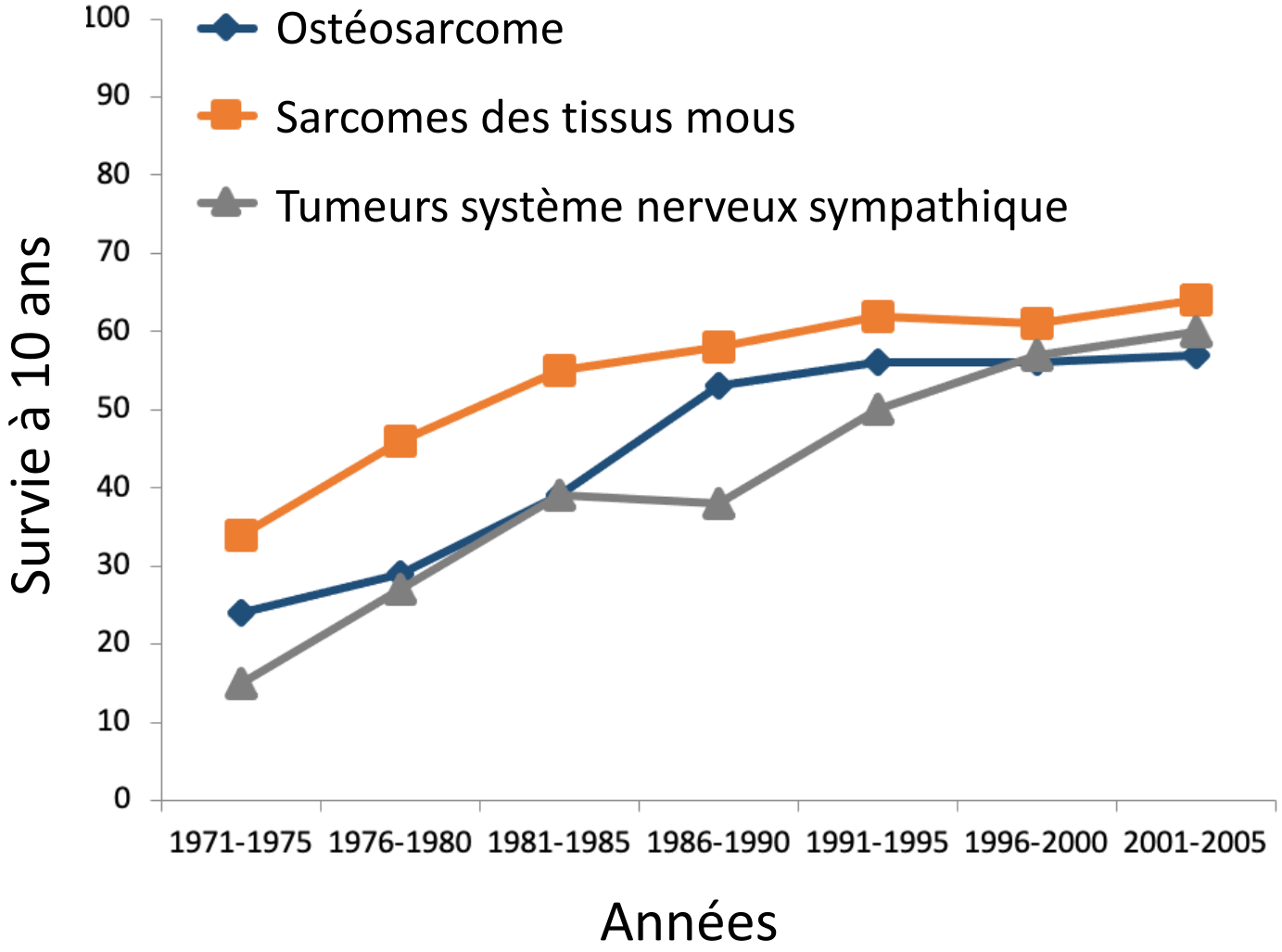
REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

Challenges en cancérologie pédiatrique





Challenges en cancérologie pédiatrique



2 CHALLENGES
Soigner PLUS et MIEUX

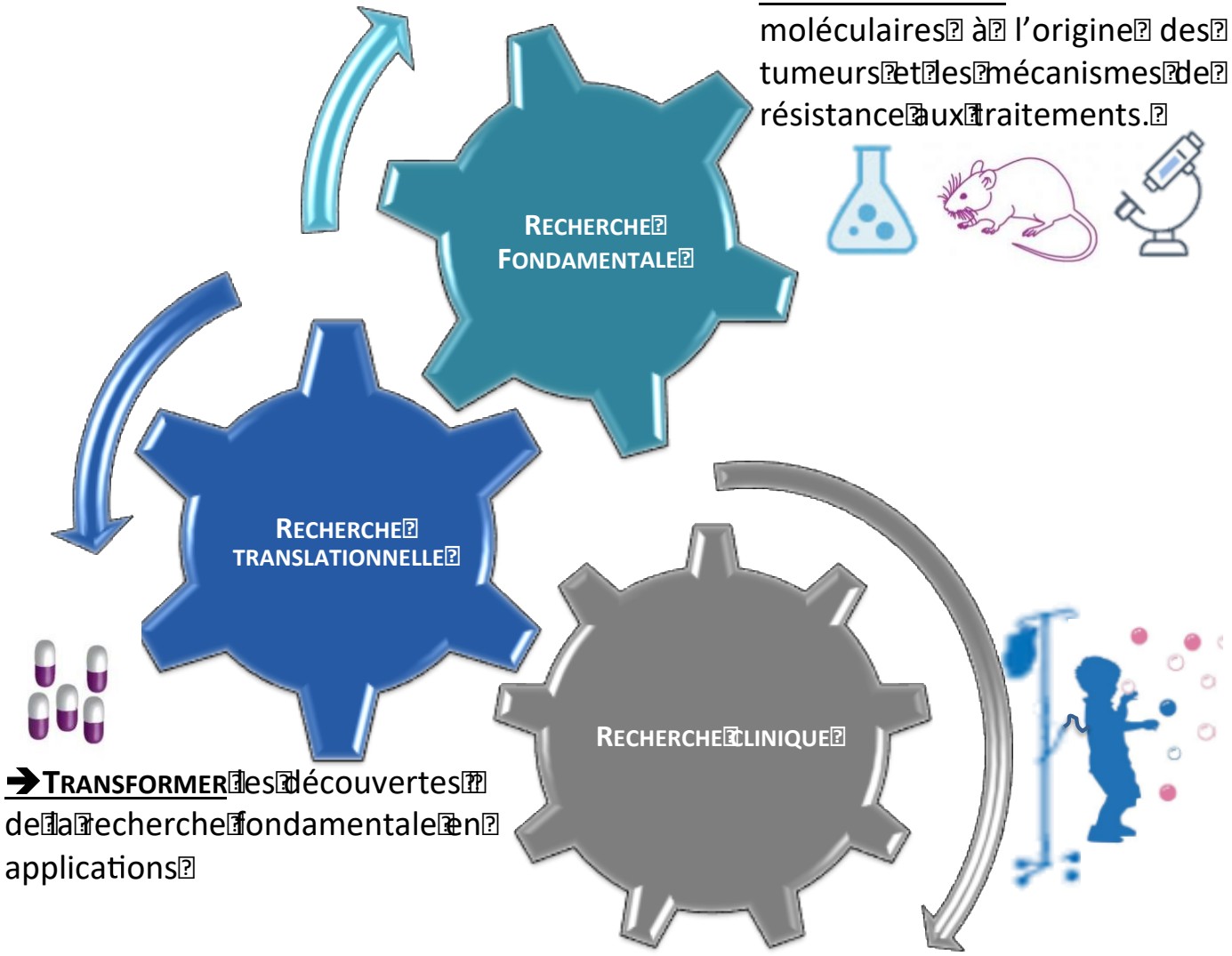
REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

Challenges en cancérologie pédiatrique

Efficacité

Disponibilité

➔ **COMPRENDRE** les bases moléculaires à l'origine des tumeurs et les mécanismes de résistance aux traitements.



➔ **TRANSFORMER** les découvertes de la recherche fondamentale en applications

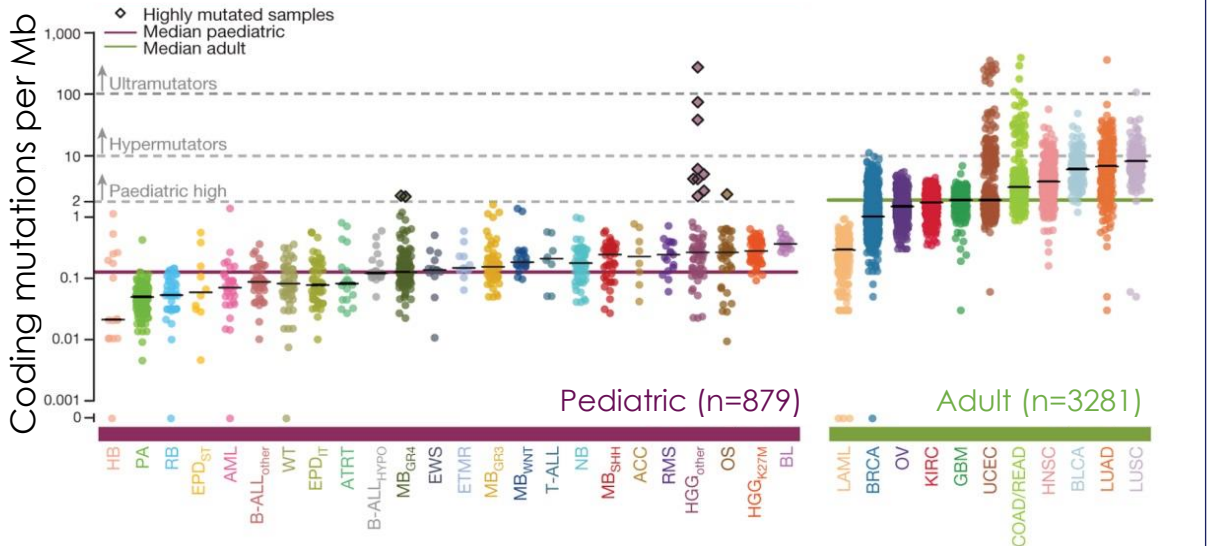
➔ **METTRE AU POINT** de nouveaux traitements

REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

Challenges en cancérologie pédiatrique

Contexte développemental

Style de vie

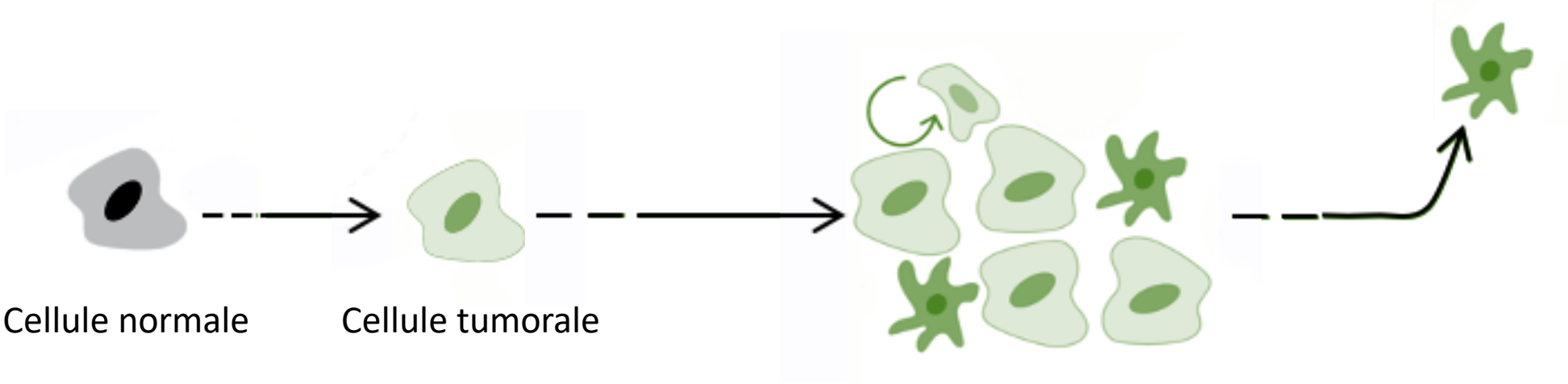


Taux de mutation

RECHERCHE DEDIEE
pour définir
leurs spécificités?

Challenges en cancérologie pédiatrique

Pourquoi et comment les cellules deviennent tumorales ?
Pourquoi et comment résistent-elles aux traitements ?

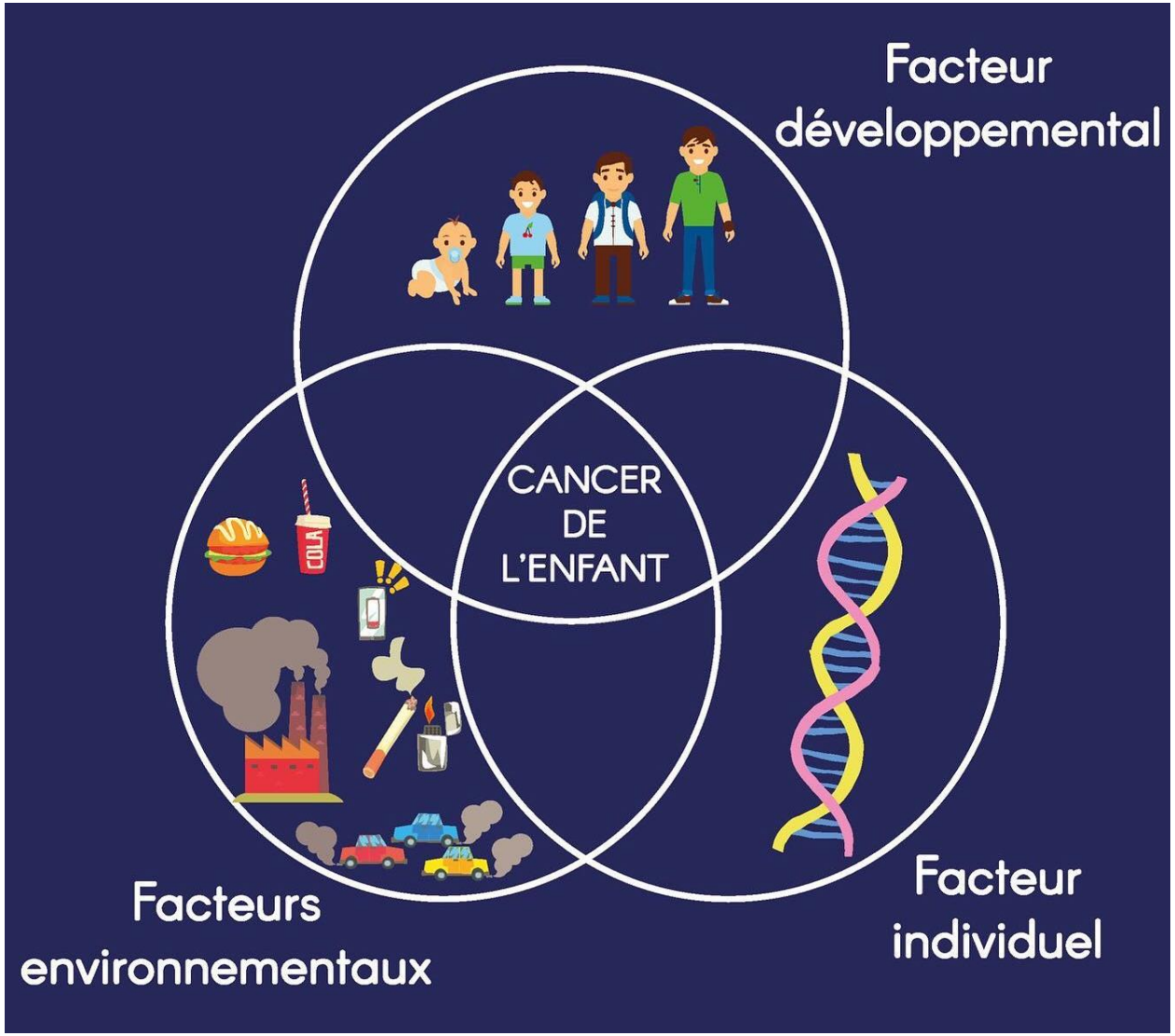


Cellule normale Cellule tumorale

Causes des cancers pédiatriques

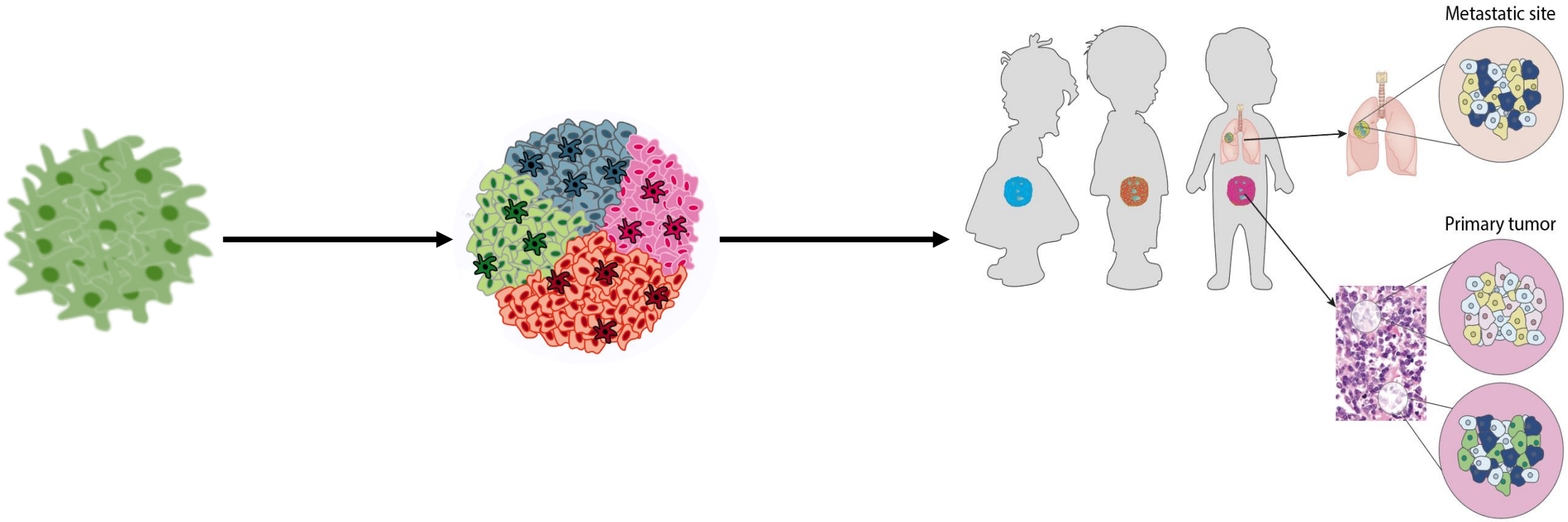
- Combinaison de facteurs à prendre en compte
- Rareté des cancers à l'échelle de la recherche

>> **Complexité** des paramètres à prendre en compte
>> **Nécessité d'une approche pluridisciplinaire**



REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

Résistance aux traitements & cancers pédiatriques



Evolution dans la perception de la complexité des cancers au cours du temps

REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

De React4Kids à Share4Kids

De React4Kids à Share4Kids

Juin, 2018

Collaborer
Partager des outils & expertises
Répondre à des problèmes communs

Mars 2023
>400 members
>40 teams

100%
of teams need omic data for their research project

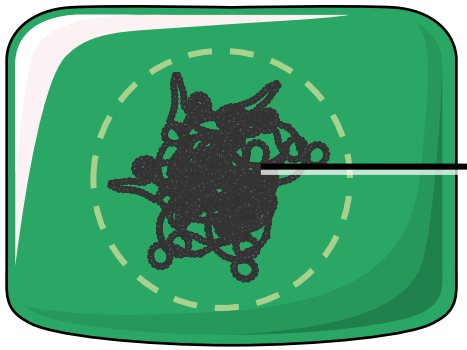
89%
use public databases as a data source

84%
can not exploit these public data

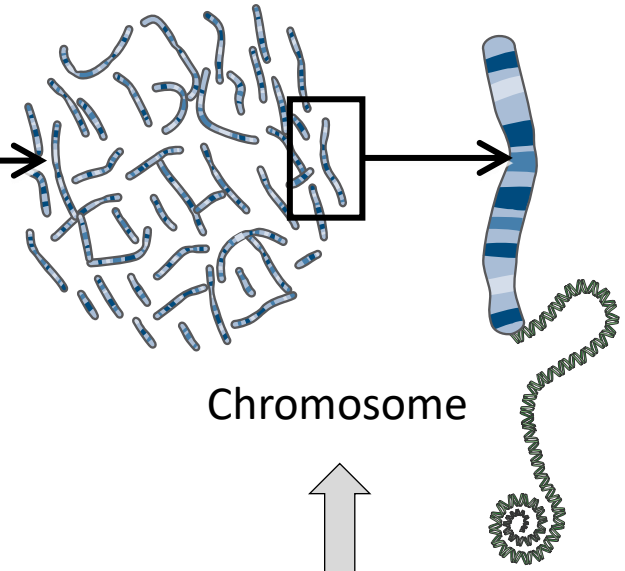
Share-4Kids

Entrepôt national de données multi-omiques

Les données multi-omiques, qu'est-ce que c'est ?



ADN



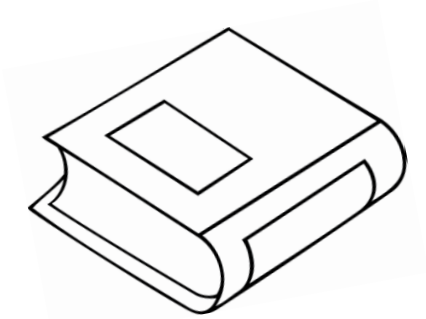
Chromosome

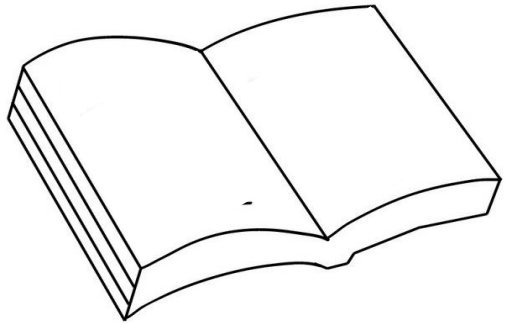
Gène

Livre

Chapitre

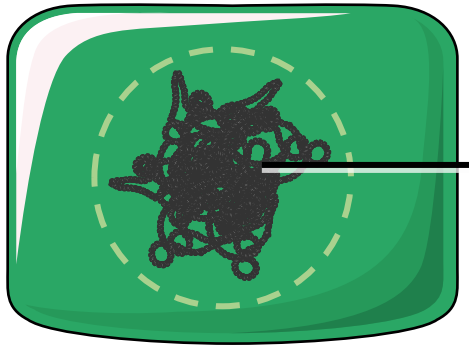
Phrase



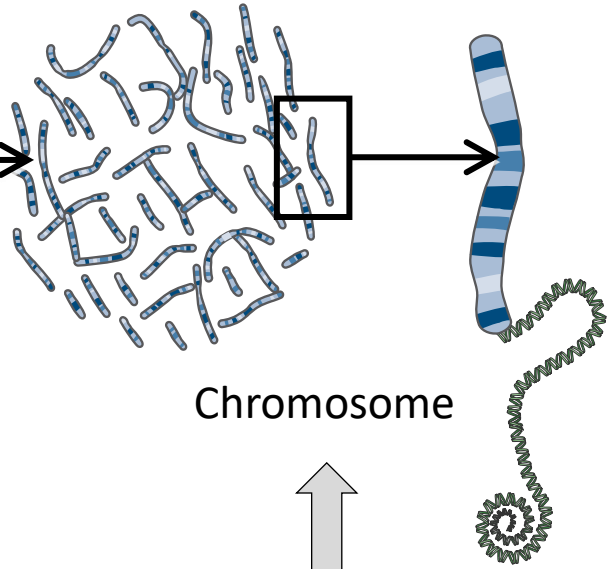


Je ne dois pas me multiplier

Les données multi-omiques, qu'est-ce que c'est ?



ADN

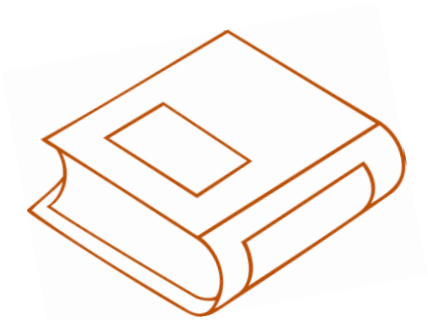


Chromosome

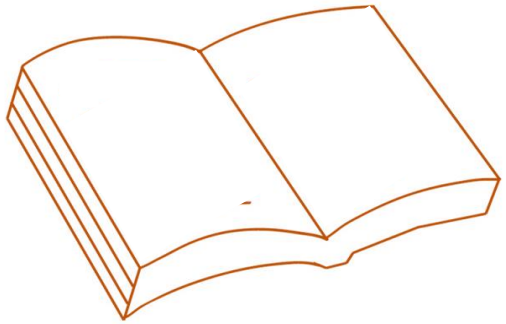
MUTATION

Gène **muté**

Livre



Chapitre

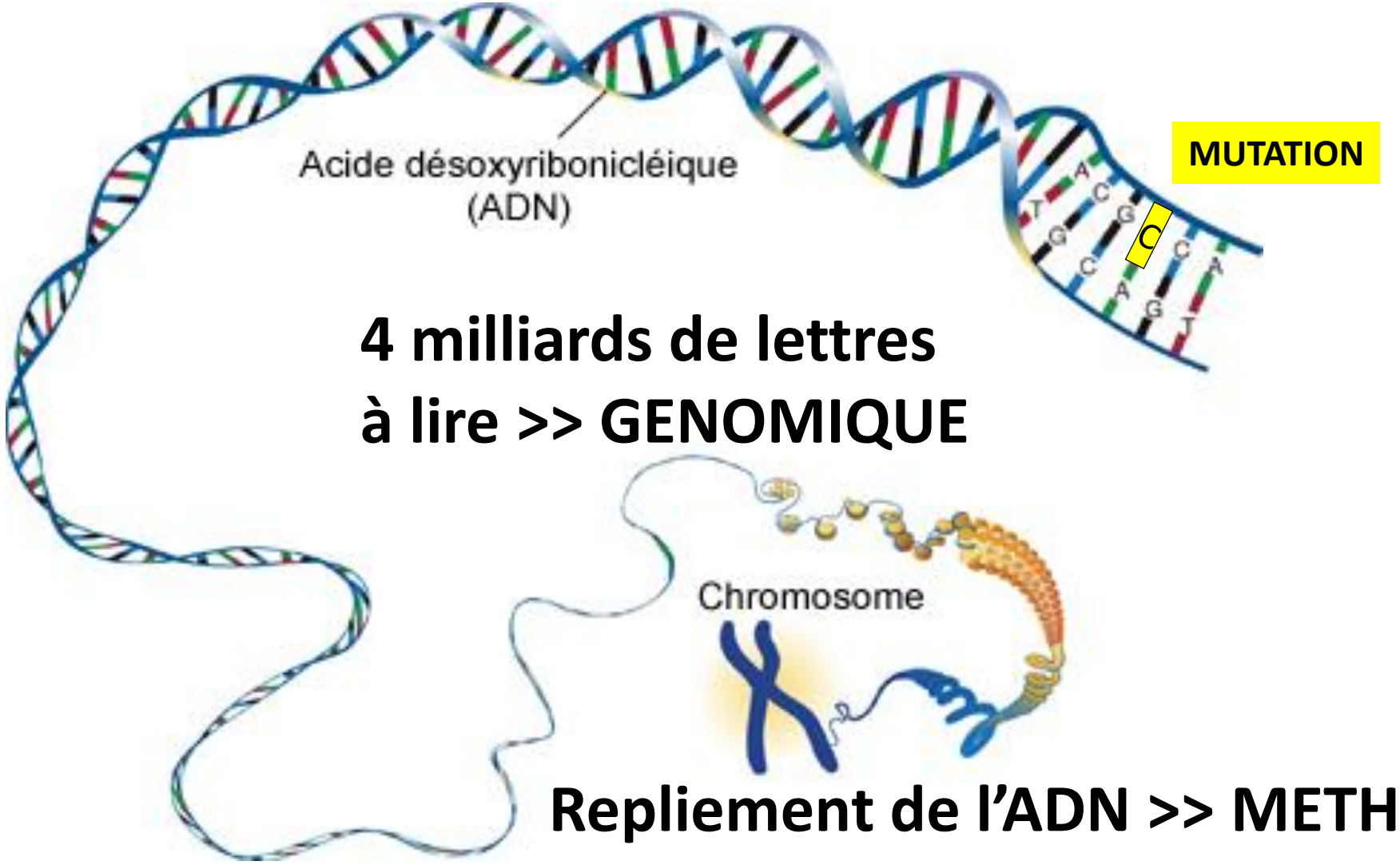


Phrase **modifiée**

Je ~~ne~~ dois ~~pas~~ me multiplier.

REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

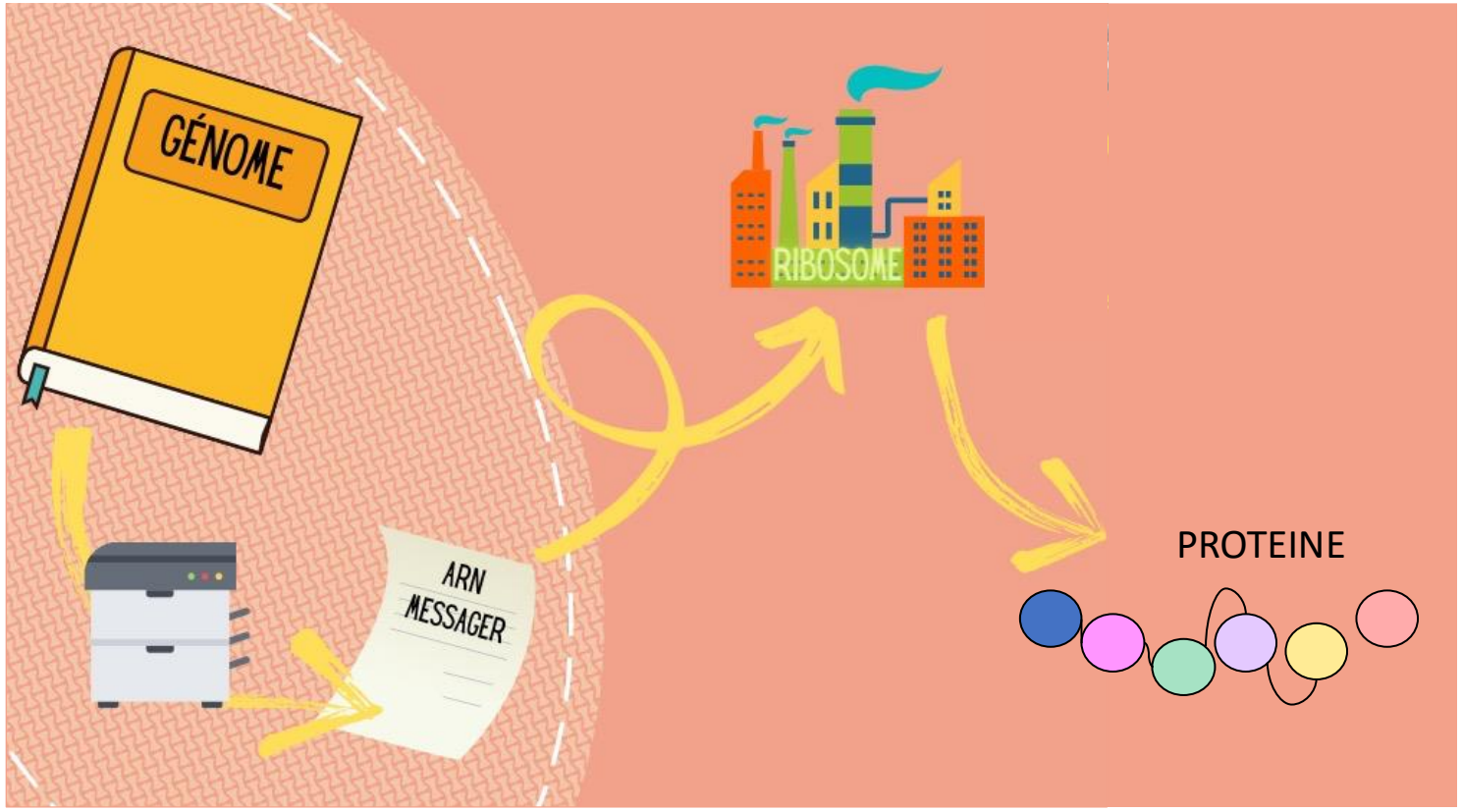
Le séquençage, une innovation majeure



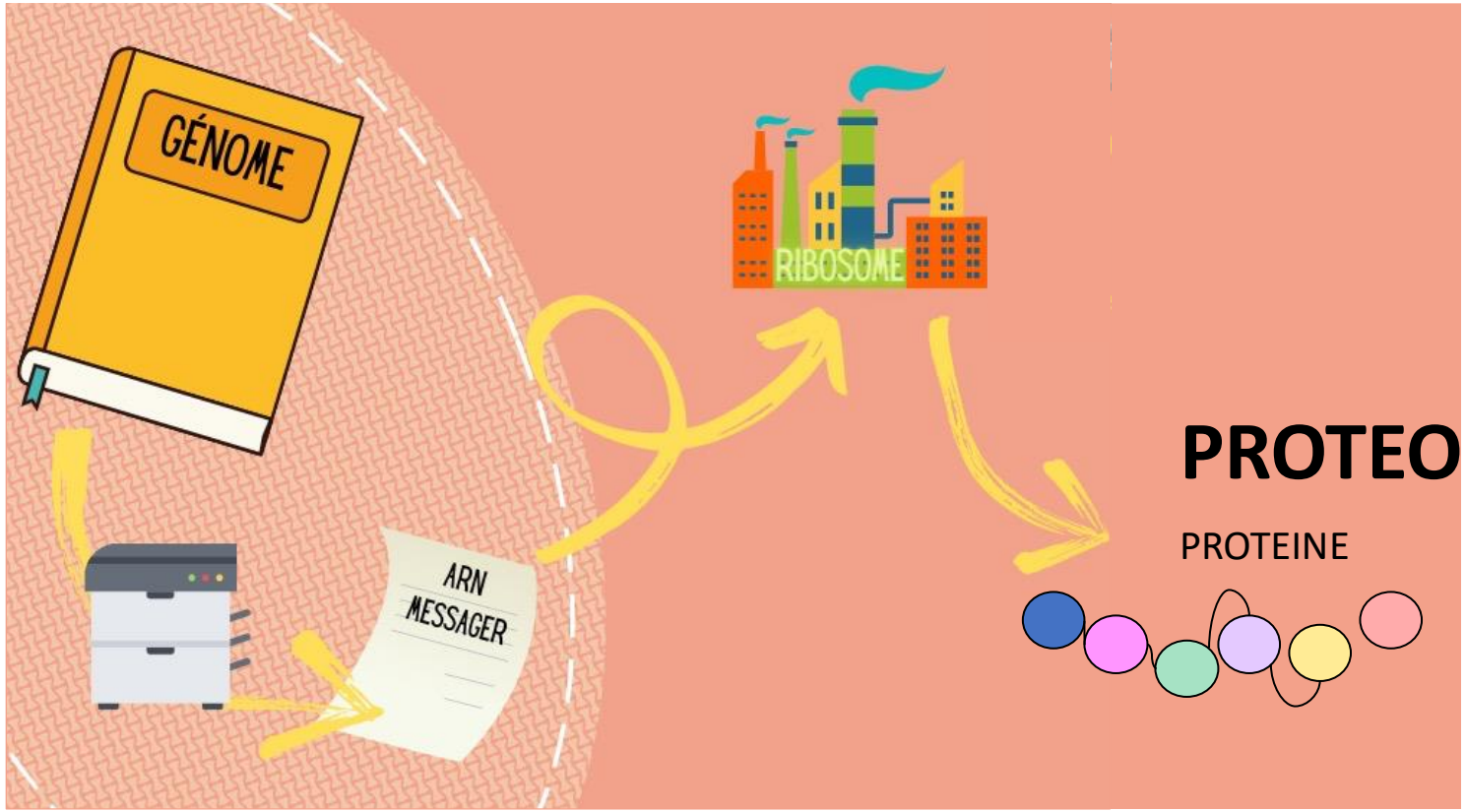
4 milliards de lettres
à lire >> GENOMIQUE

Repliement de l'ADN >> METHYLOME

Le séquençage, une innovation majeure

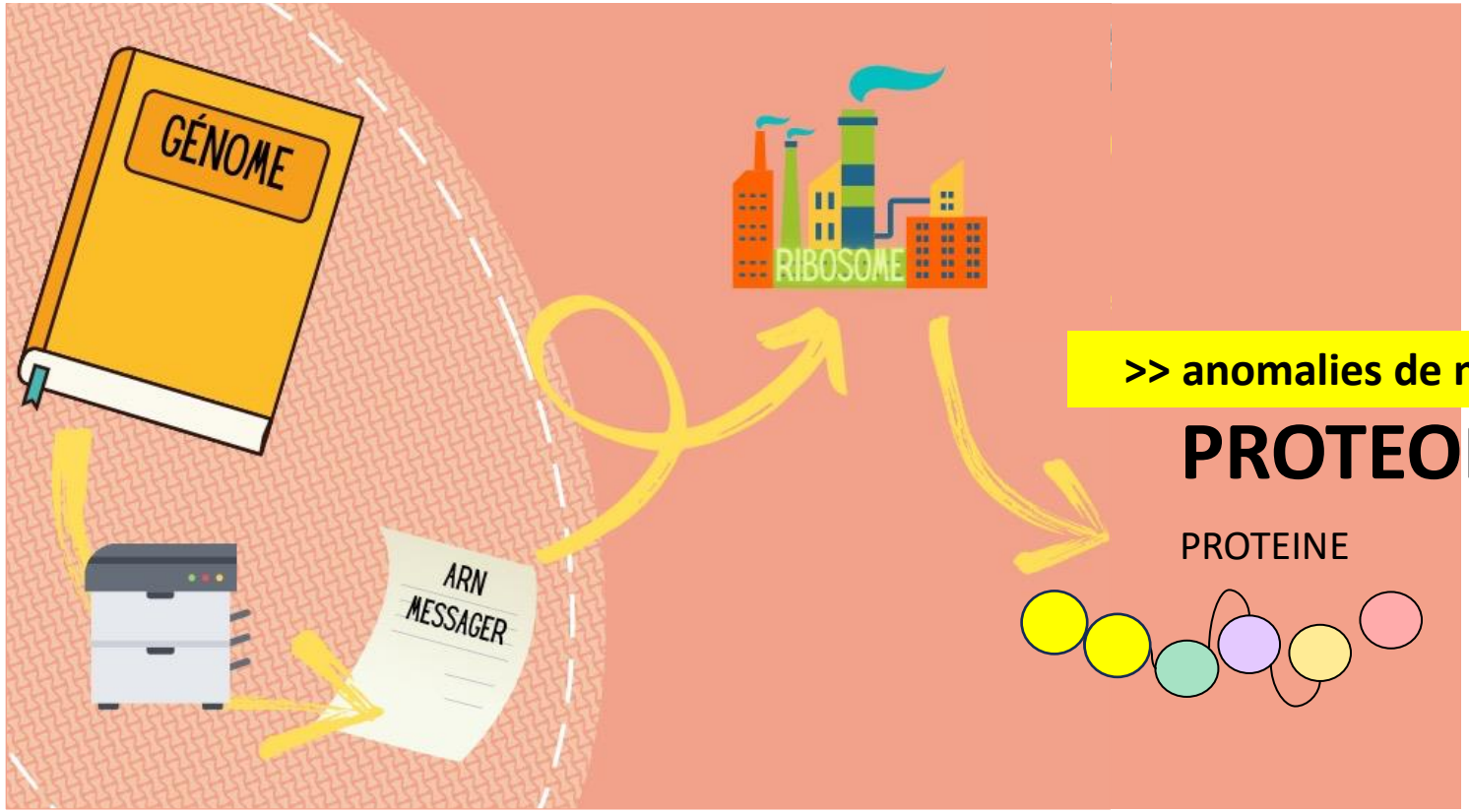


Le séquençage, une innovation majeure



TRANSCRIPTOMIQUE

Le séquençage, une innovation majeure



>> anomalies de nombre/de type

PROTEOMIQUE

PROTEINE

TRANSCRIPTOMIQUE

>> anomalies de nombre/de type

Apport des données multi-omiques

Causes des cancers pédiatriques ?

Biologistes du développement

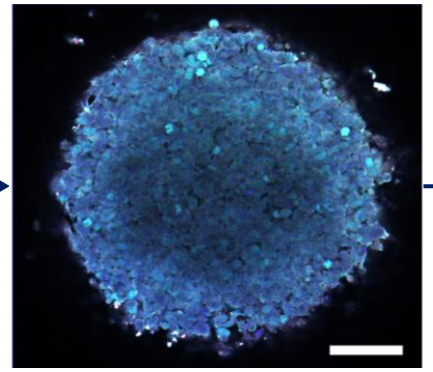
Altérations génétiques
(Ras^{Mutant}, +/-Hh, +/-?...)

Myoblastes

MSCs

Autres ?

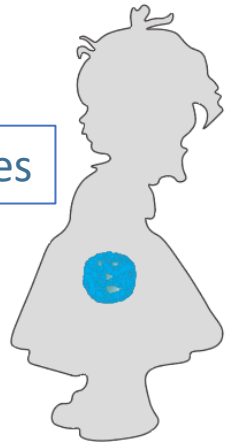
Polluants



Signature
Multi-omique
d'exposition

Bioinformaticiens

Epidémiologistes

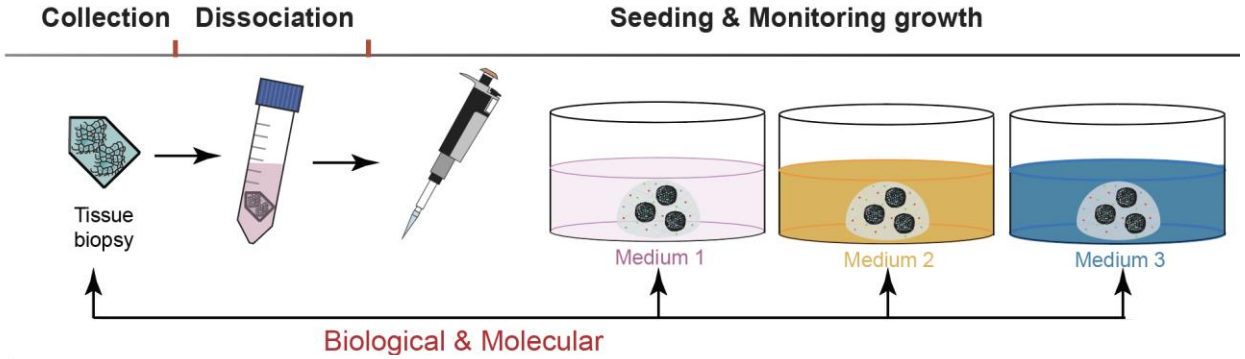


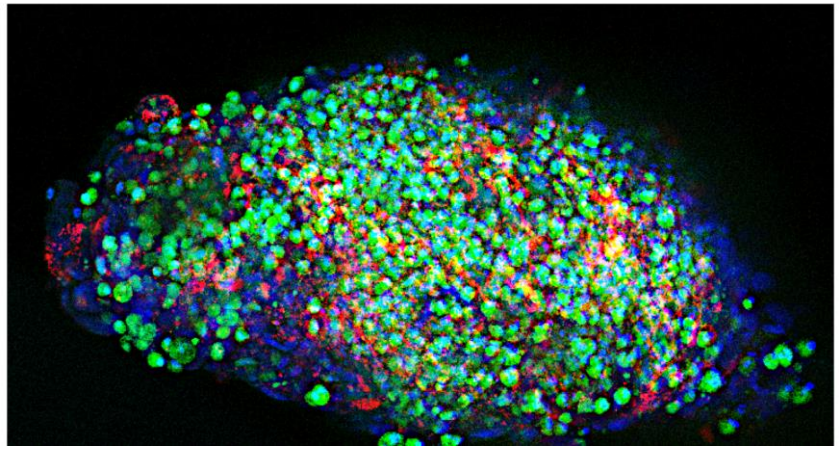
Identification d'une signature d'exposition ?
Corrélation avec l'environnement ?

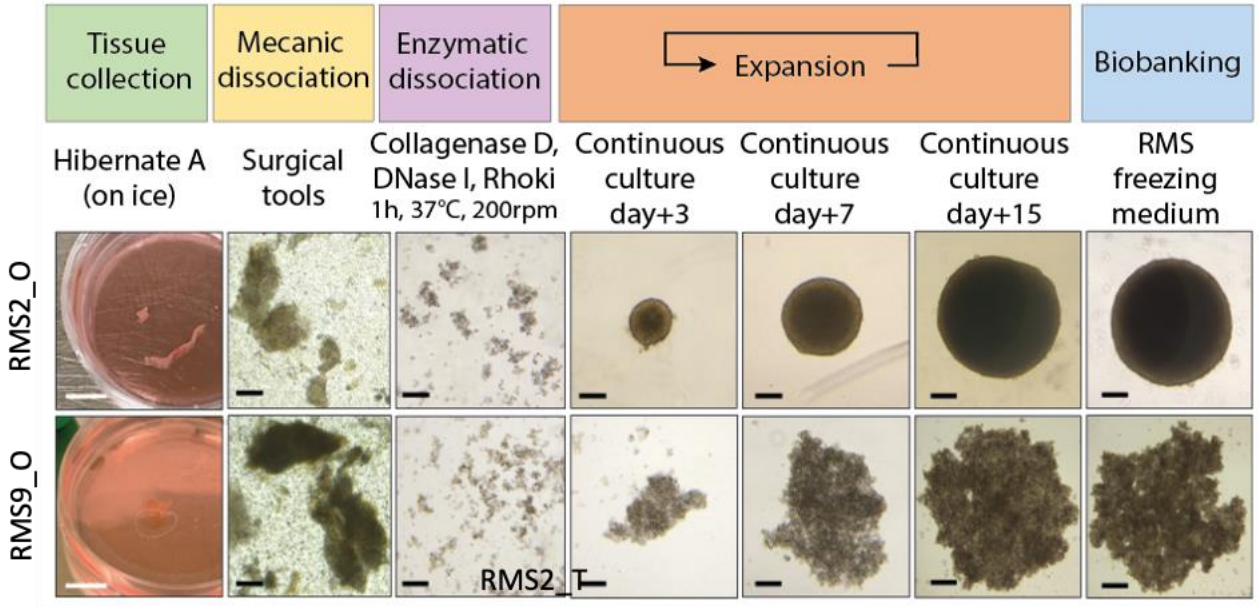
>> Besoin de données multi-omiques sur les patients et les modèles <<

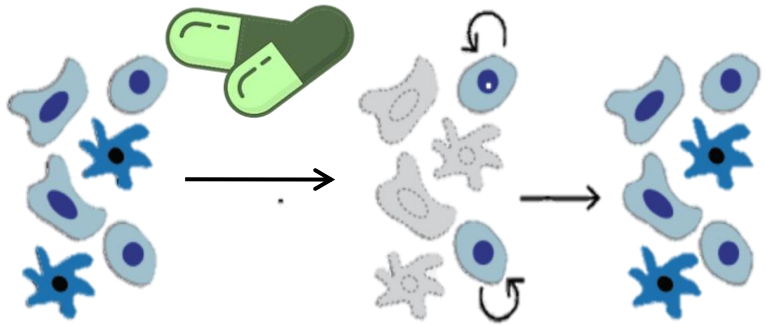
Apport des données multi-omiques

Causes des résistances?









>> Besoin de données multi-omiques sur les patients et les modèles <<


NovaSeq 6000
illumina

REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

Share4Kids: 1er entrepôt national de données multi-omiques

Public Data

New Data

Raw SQL

(i) Single -omics

(ii) Multi -omics integration

(iii) System's response to treatment

PATIENTS

MODELS

Chromatin

DNA

Transcripts

Proteins

COMPARISON

sensitive vs resistant

metachronous samples

(iv)

Patients/models cross-dataset analyses

DRUG DISCOVERY

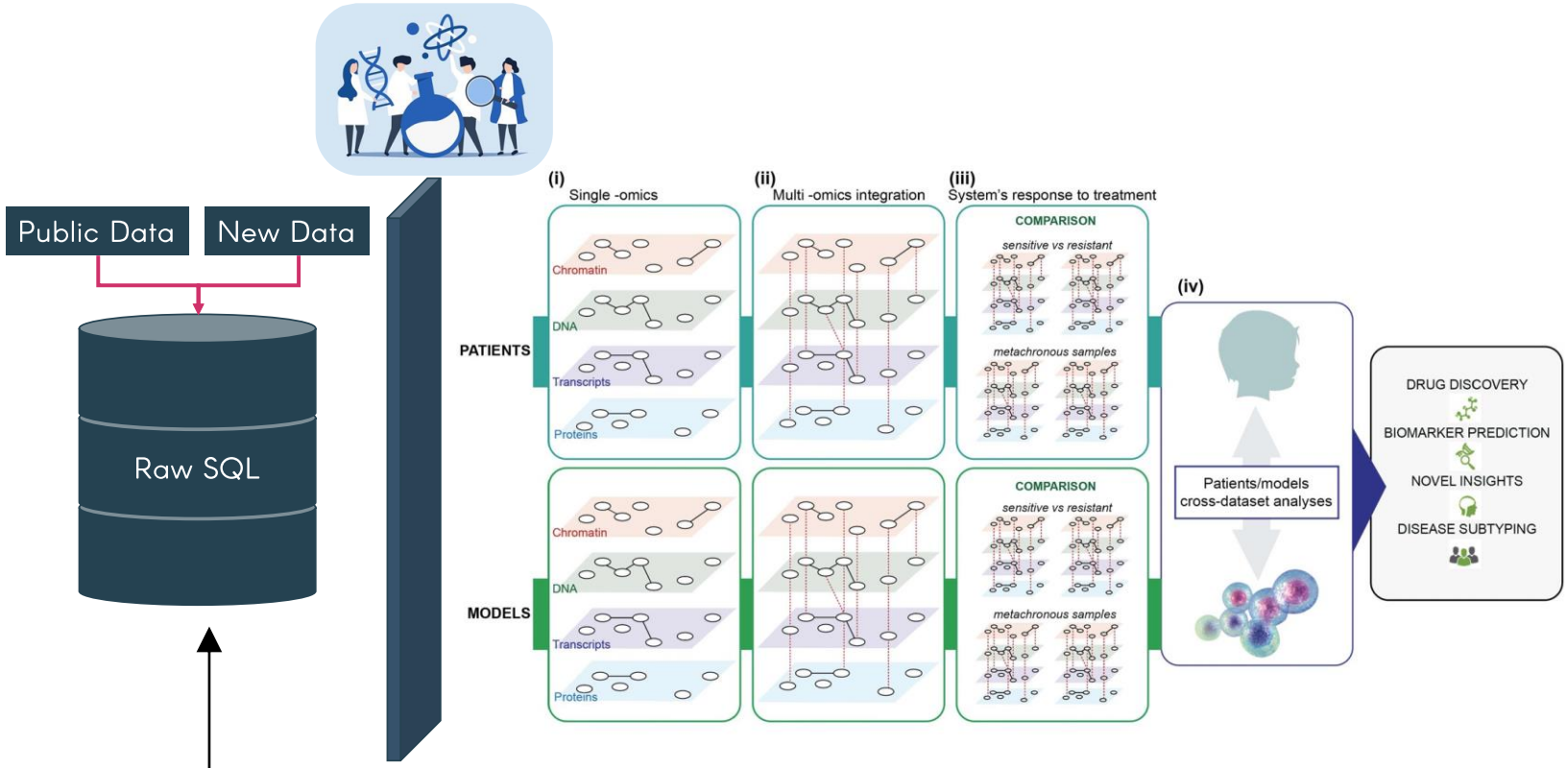
BIOMARKER PREDICTION

NOVEL INSIGHTS

DISEASE SUBTYPING

REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

Share4Kids: 1er entrepôt national de données multi-omiques



PHASE 1: Signatures moléculaires de 150 tumeurs de patients

PHASE 1: Interface d'accès de niveau 1

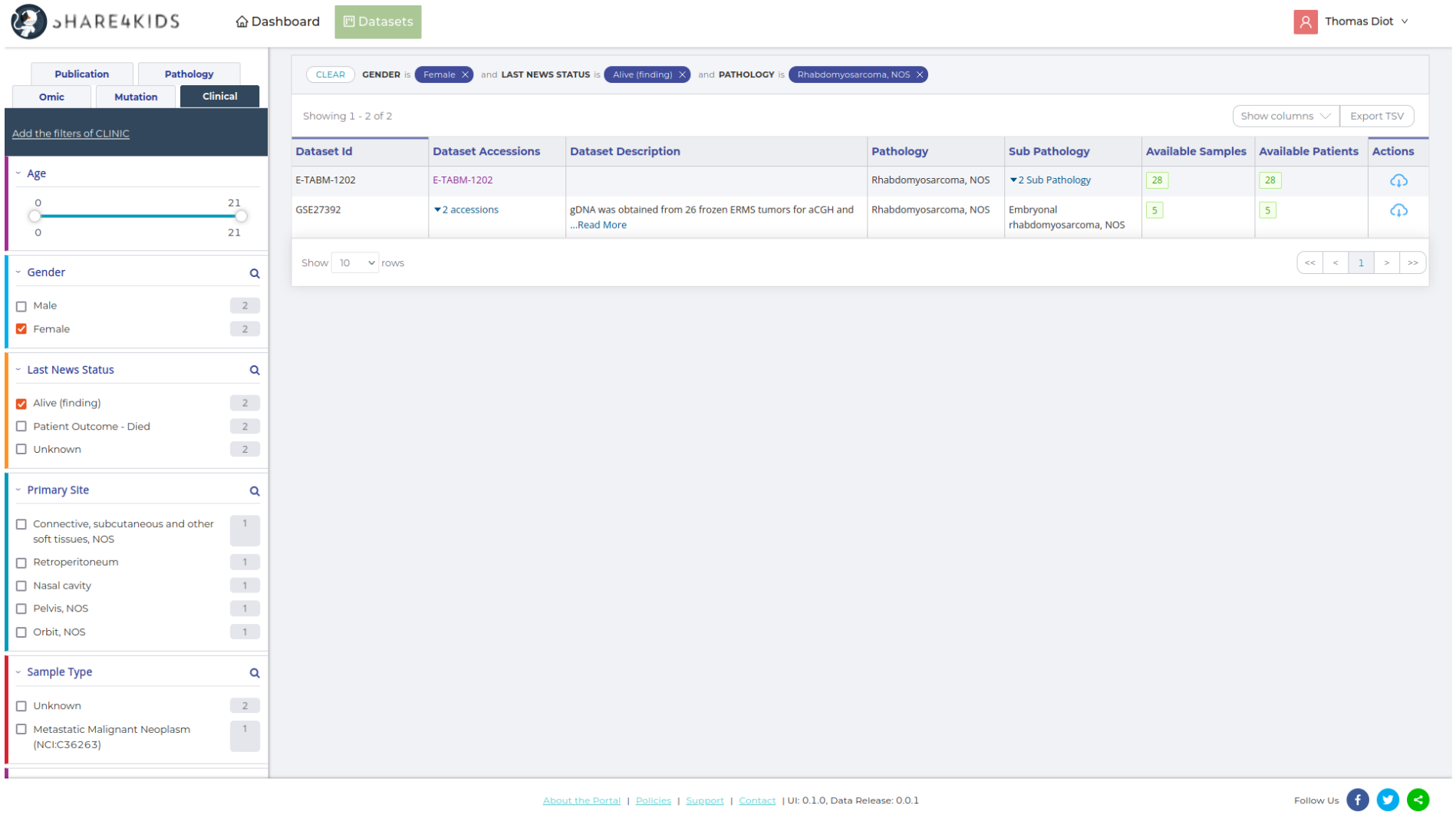
REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

Share4Kids: 1er entrepôt national de données multi-omiques

PHASE 1

Login

Autorisation



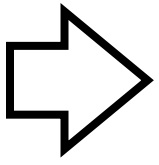
REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

Share4Kids: 1er entrepôt national de données multi-omiques

PHASE 1

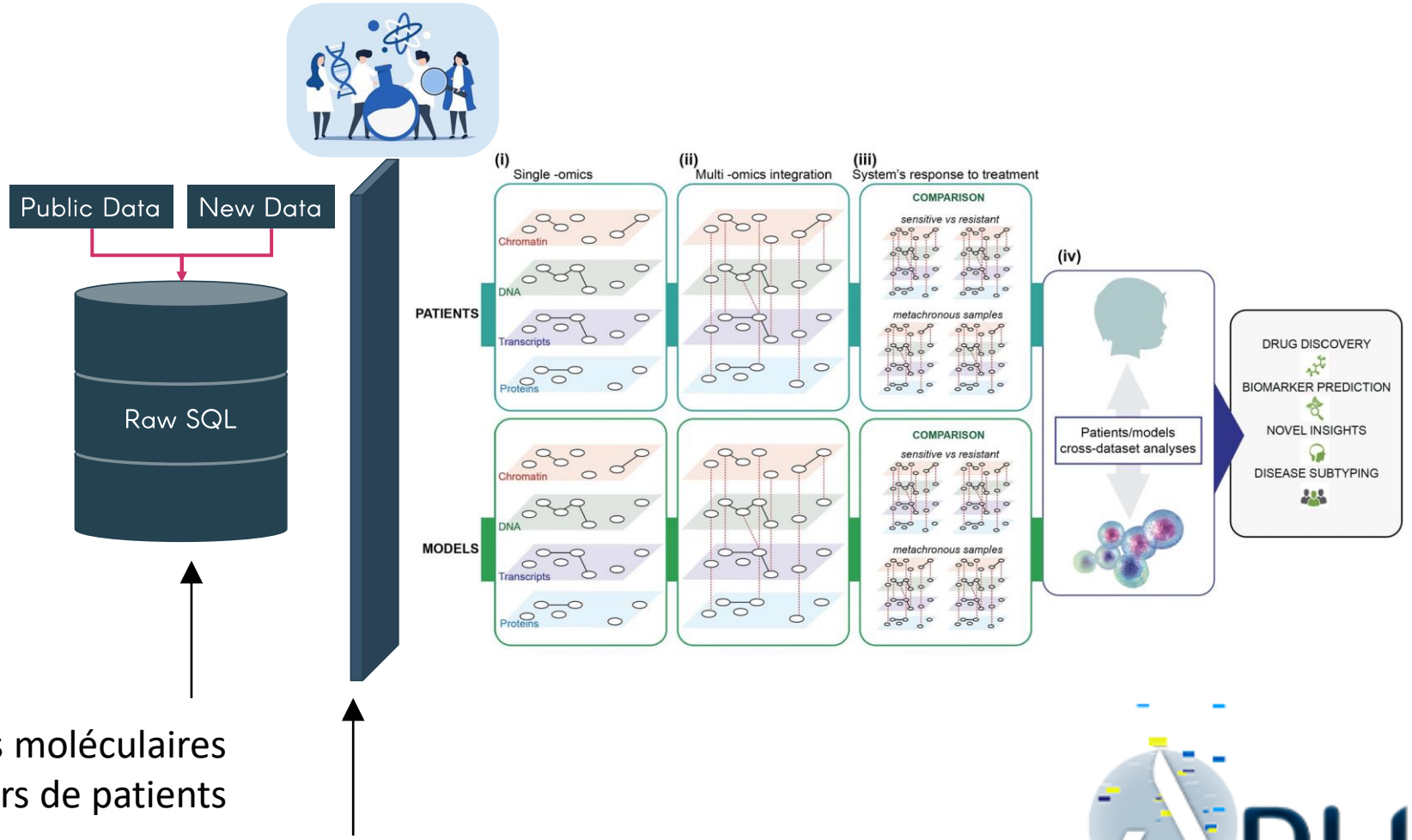
Login

Autorisation



	A	B	C	D	E	F	G	H	I	J	K	L	M	N	O	P	Q	R
1		RMSC005	RMSC006	RMSC009	RMSC010	RMSC012	RMSC015	RMSC017	RMSC026	RMSC027	RMSC029	RMSC032	RMSC033	RMSC034	RMSC035	RMSC038	RMSC039	RMSC041
2		RMS005	RMS006	RMS009	RMS010	RMS012	RMS015	RMS017	RMS026	RMS027	RMS029	RMS032	RMS033	RMS034	RMS035	RMS038	RMS039	RMS041
3		12	5,8	3	17,3	3,4	19	15,2	3,8	1,9	0,5	4,5	16,5	5,5	11,7	12,1	2,5	0,8
4		Unfavourabl	Favourable	Favourable	Unfavourabl	Favourable	Unfavourabl	Unfavourabl	Favourable	Favourable	Unfavourabl	Favourable	Unfavourabl	Favourable	Unfavourabl	Unfavourabl	Favourable	Unfavourabl
5		ARMS	ARMS	ARMS	ARMS	ERMS	ARMS	ARMS	ARMS	ARMS	ARMS	ARMS	ARMS	ARMS	ARMS	ARMS	ARMS	ERMS
6		limb	Genitourinar	Genitourinar	no primary t	Parameninge	Parameninge	Parameninge	other	Genitourinar	limb	limb	Parameninge	limb	limb	Parameninge	Parameninge	Genitourinar
7		M0	M0	M0	M1	M0	M1	M0	M1	M0	M0	M0	M1	M1	M1	M0	M1	M0
8		8,25	5,33	5,17	2,08	4,42	1,25	2,58	2,58	5,25	2,5	4,67	3,08	1	5,58	4,42	1,33	4,08
9		alive	alive	alive	dead from di	alive	dead from di	dead from di	dead from di	alive	dead from di	dead from di	dead from di	dead from di	dead from di	alive	dead from di	alive
10		Pax3	Neg	Neg	Pax3	Neg	Pax3	Pax3	Pax3	Neg	Ncoa1	Pax3	Pax3	Pax3	Pax3	Neg	Neg	Neg
11		INTERMEDIA	INTERMEDIA	INTERMEDIA	HIGH RISK	NA	HIGH RISK	INTERMEDIA	HIGH RISK	INTERMEDIA	INTERMEDIA	INTERMEDIA	HIGH RISK	HIGH RISK	HIGH RISK	INTERMEDIA	HIGH RISK	LOW RISK
12																		
13	A1BG	5,26541693	6,10804293	5,87819674	5,60907478	6,1132609	5,82251394	5,7886511	5,08550292	5,37086779	5,70411506	5,03114844	5,04468208	5,23963542	5,49938243	4,91961391	5,42559999	5,72683693
14																		
15	A1BG-AS1	5,06414078	5,15035126	5,14249041	4,82165681	4,91979772	5,03809485	5,17305716	4,77730945	4,88166349	5,11211804	5,03428401	4,71178107	4,94407741	4,93125932	5,02098717	5,18707919	4,93014041
16																		
17	A1CF	3,99437905	3,96920416	3,95018741	4,10385366	4,03951325	3,99807568	4,08101226	3,92644226	4,15716708	3,74519613	3,87438364	4,00733545	3,97411102	3,94602199	3,74579911	3,84303463	3,89433437
18																		
19	A2M	7,53043421	8,11419284	7,34470685	8,59625113	7,4269053	7,68868081	7,80240853	7,09247925	7,88597118	7,15734997	7,3949805	7,81253951	7,15274608	7,98262169	7,21375067	7,27338013	7,95483536
20																		
21	A2M-AS1	4,31817723	5,00741607	3,85875177	4,66882381	3,80583087	4,38211282	4,64877137	5,05790331	6,44223971	4,38323924	5,80233427	5,57121258	4,53881405	6,24326201	6,43680204	4,07796916	4,44206105
22																		
23	A2ML1	3,83620481	3,75374786	3,9309522	3,93725719	4,00738191	3,77596368	4,00842519	4,04487646	3,7617115	3,85196896	3,94171877	3,99516914	3,80857741	3,91085744	6,27972119	4,95556429	4,61278373
24																		
25	A2MP1	4,76375111	5,04492608	4,53469063	5,21603112	4,70551593	4,90738883	4,63040168	4,81277045	4,90445997	4,66157501	5,11781167	5,01978692	4,85496066	4,78167337	4,59172036	4,74723956	4,95203124
26																		
27	A4GALT	6,01042354	6,06604361	6,32692912	6,00583917	6,42710896	6,4252868	6,14348918	5,75943659	6,26081901	5,87642377	5,78337967	5,87848624	5,88042938	6,29728724	6,37603811	6,24376252	5,82693536
28																		
29	A4GNT	4,22609998	4,27099385	4,44371904	4,38278316	4,18503079	4,71611685	4,4095989	4,29918653	4,34502749	4,07110529	4,08635331	4,1929592	4,1169925	4,11742866	4,11219297	4,11819481	4,27872549
30																		
31	AA06	4,75838015	4,66816125	4,96189561	4,96193738	4,84899385	5,18826457	4,80296799	5,23800071	4,66957163	4,71641008	4,72025292	4,6265799	4,58269367	4,73649617	4,59954879	4,84683241	4,894491
32																		
33	AAAS	7,07564614	7,63394688	7,48640212	7,72172161	7,31928787	7,55582575	7,41632151	7,55180531	7,44331075	7,04477262	7,52367391	7,10768537	7,16246741	7,01798102	6,66792386	6,8119467	7,38768593
34																		
35	AACS	8,78066014	8,08624801	8,1067937	7,40172707	7,98333098	7,1585093	8,64008264	8,24355122	7,78364391	7,36988331	9,04968239	7,40012385	7,68521793	7,38938723	8,17405076	7,87582088	8,31398809
36																		
37	AACSP1	3,57825712	4,82967315	3,91119739	6,02961617	5,48672709	5,06851591	3,78305575	3,68130683	3,380645	7,22006753	6,34475069	3,88885106	3,70716378	3,58217035	3,40212119	3,44817685	3,57417202
38																		
39	AADAC	4,61583121	4,50853107	4,291673	4,84530908	4,73926148	4,59506876	4,3084475	4,45778316	4,19497922	5,83993912	4,4621993	4,474166	4,27731964	4,56512291	6,66143425	5,33549352	4,12501968
40																		
41	AADACL2	3,00197896	2,96156836	3,23845419	3,19927405	3,10748338	3,06611212	3,12875581	3,11093805	3,16248102	3,29533335	2,84107058	3,0069498	3,00266043	3,03375344	3,48413112	3,28158093	3,11760111
42																		
43	AADACP1	3,22632431	3,56470758	3,42506022	3,57999731	4,21342409	3,47521382	3,2649911	3,28795446	3,42237398	3,32952309	3,24917108	3,4426049	3,22892094	3,26859163	4,63153074	4,0924398	3,19276509
44																		
45	AADAT	7,15484199	6,74775557	7,17331517	6,97917665	7,23708138	6,97719089	7,03006564	7,1196233	6,89572004	7,20798385	7,63980789	6,77546205	6,75654412	6,7238146	5,25528993	5,08254306	6,79359424
46																		
47	AAED1	7,0913036	6,15088999	6,60229831	6,69219859	6,97270695	6,7727752	7,12938076	6,46823938	7,68204708	6,14095814	6,66926232	6,88841027	6,45165746	7,33174836	6,71809103	7,69859829	6,62439749

Share4Kids: 1er entrepôt national de données multi-omiques

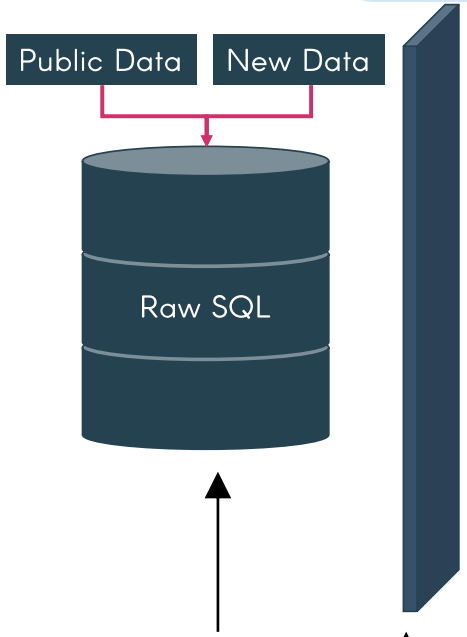


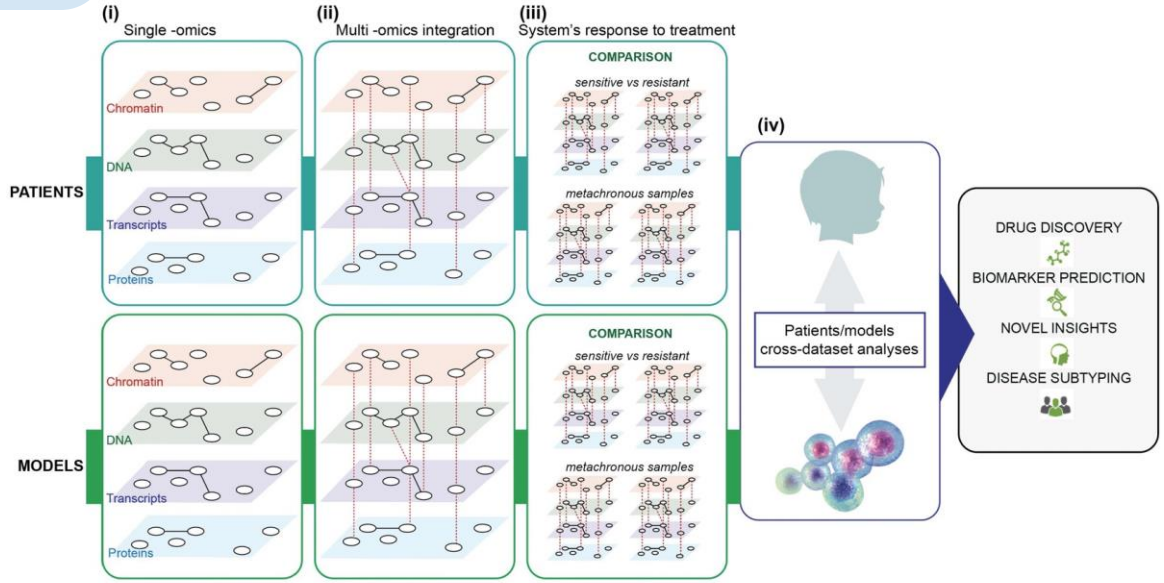
PHASE 1: Signatures moléculaires de 150 tumeurs de patients

PHASE 1: Interface d'accès de niveau 1

PHASE 2: Interface d'accès de niveau 2 avec des outils d'analyse

Share4Kids: 1er entrepôt national de données multi-omiques





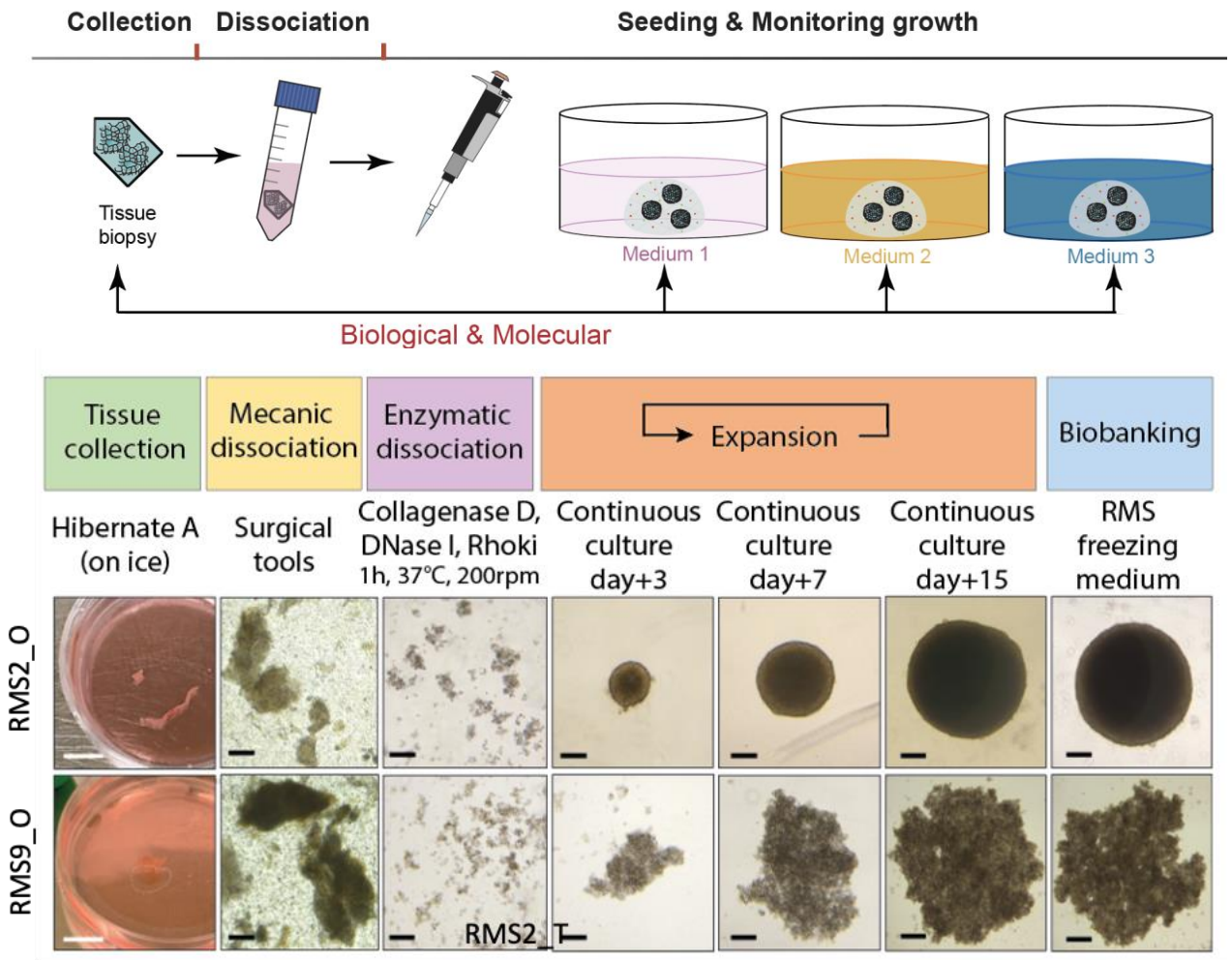
PHASE 1: Signatures moléculaires de 150 tumeurs de patients

PHASE 1: Interface d'accès de niveau 1

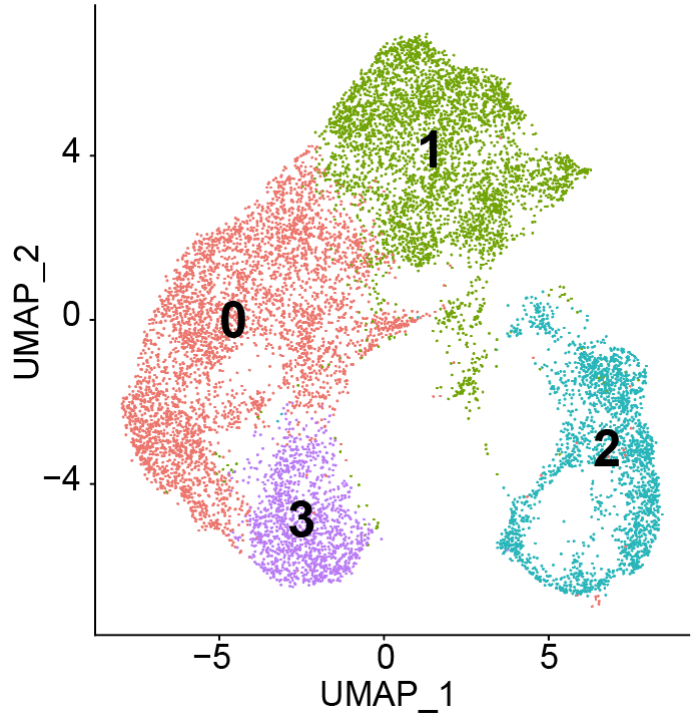
PHASE 2: Séquençage single-cell de tumeurs et de modèles pré/post-traitements

PHASE 2: Interface d'accès de niveau 2 avec des outils d'analyse

Apport des données single-cell

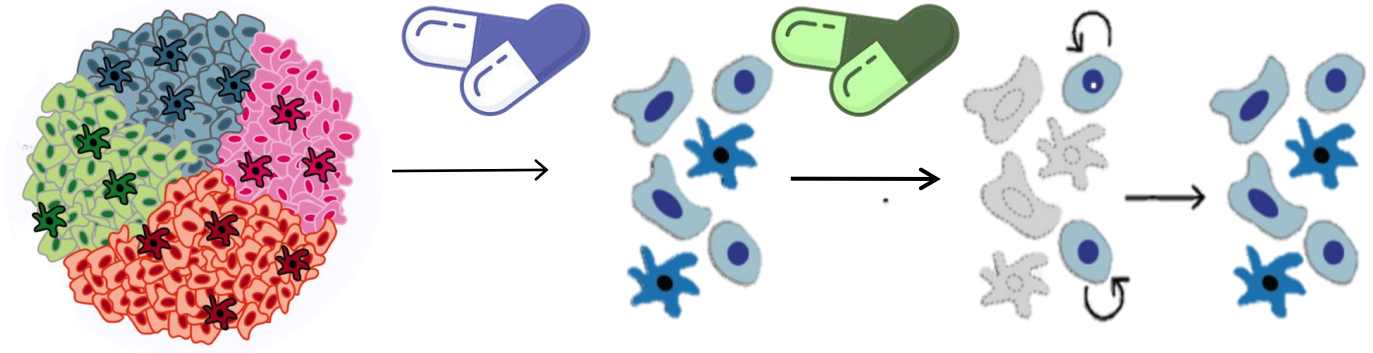


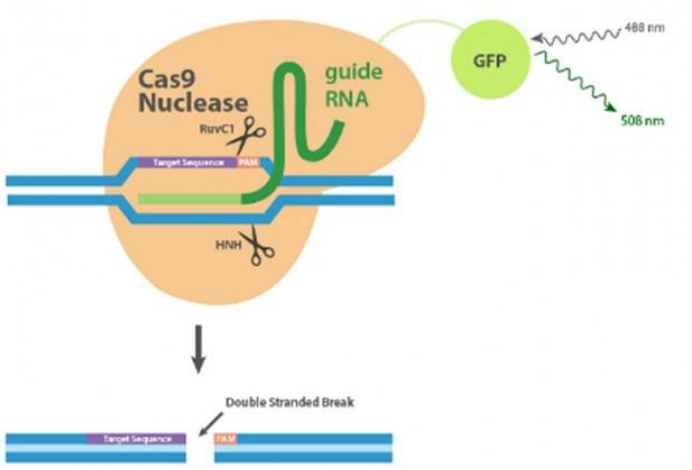
Identification des populations de cellules tumorales par séquençage single-cell



REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

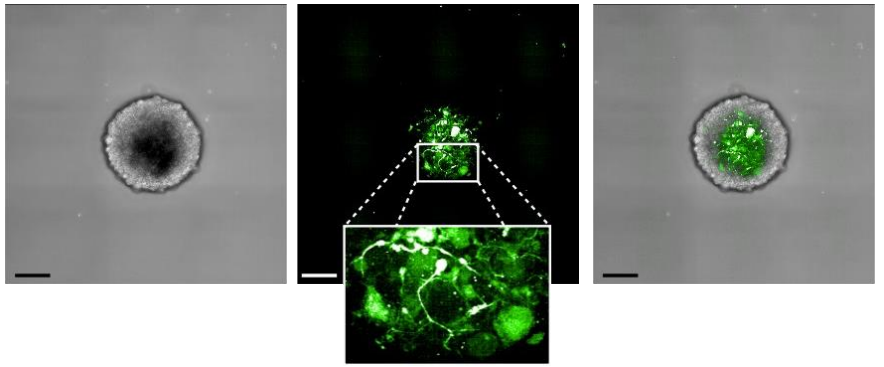
Apport des données single-cell et du CRISPRCas9





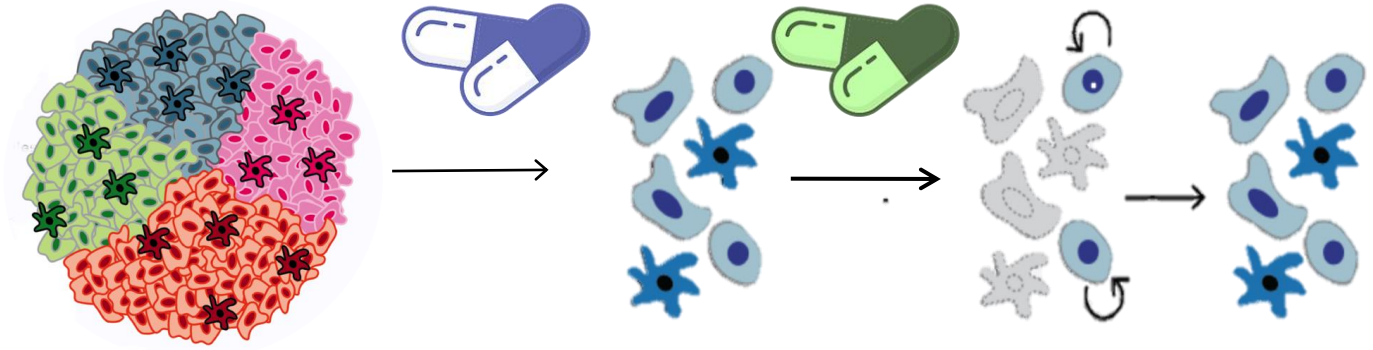
Technique de CRISPRCas9

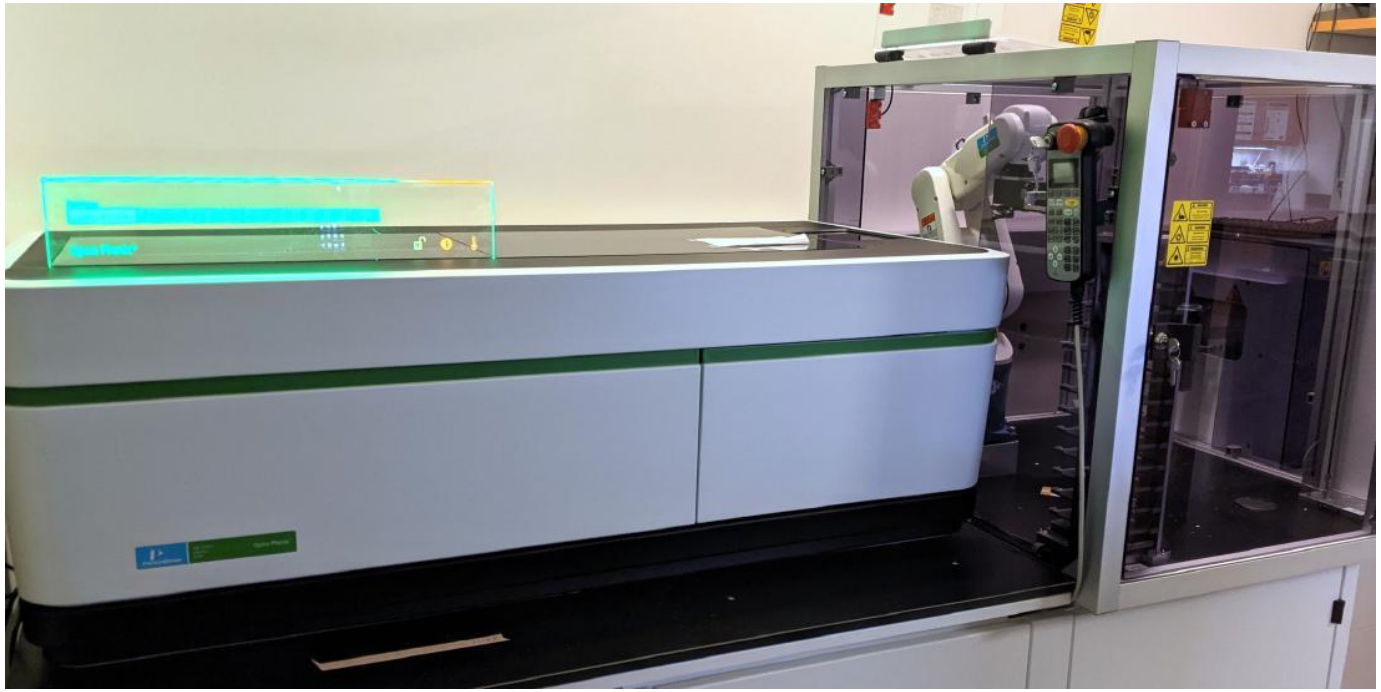
Dissociation → Electroporation → Sorting → Sequencing

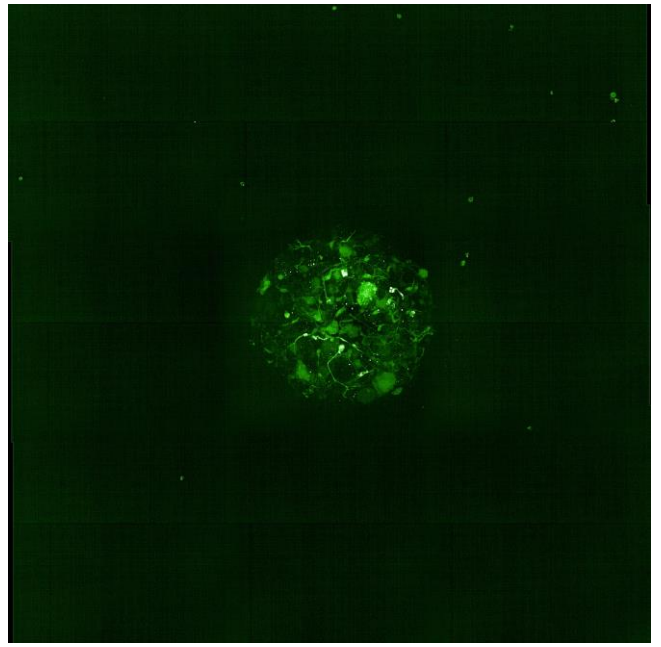


REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

Apport des données single-cell, du CRISPRCas9 Et de l'imagerie 3D !

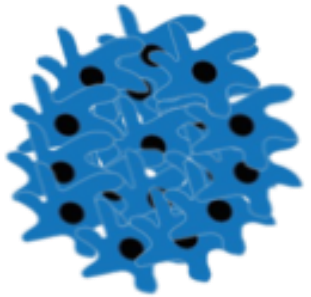




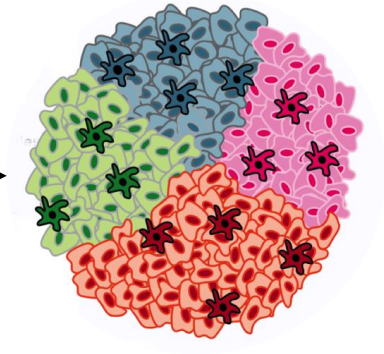


REACT-4KIDS!
Fundamental Research in pediatric Oncology Network

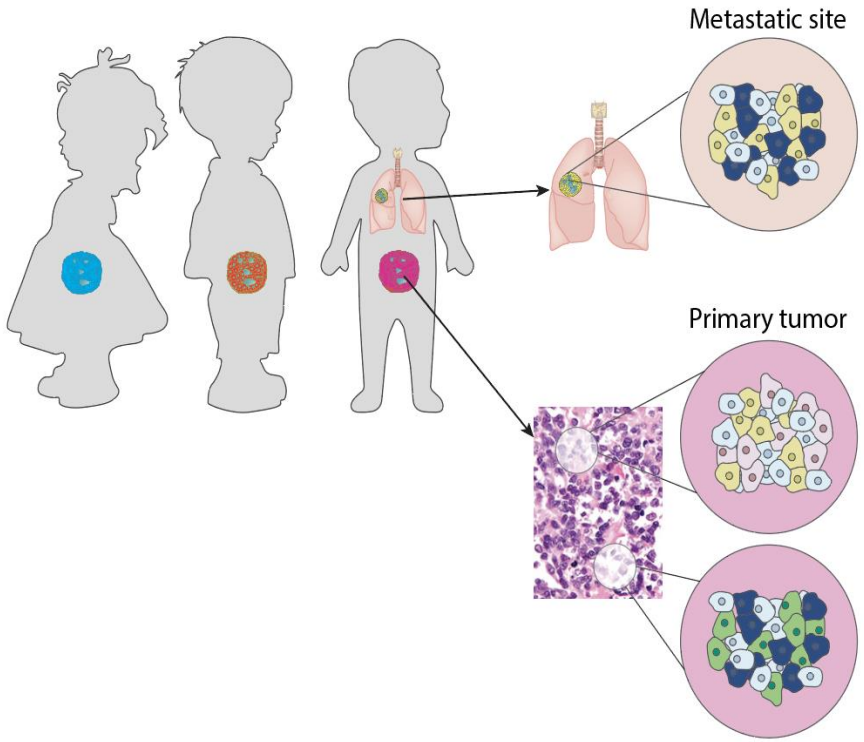
Apport des données multi-omiques



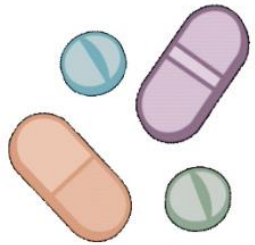
2.500€



5.000€



Coût des séquençages multi-omiques sur tumeurs entières et en single-cell



Comprendre pour Soigner

Les cancers des enfants et des jeunes

MERCI !