
CM01 BEAMLINE UPDATES

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Photo by Cande

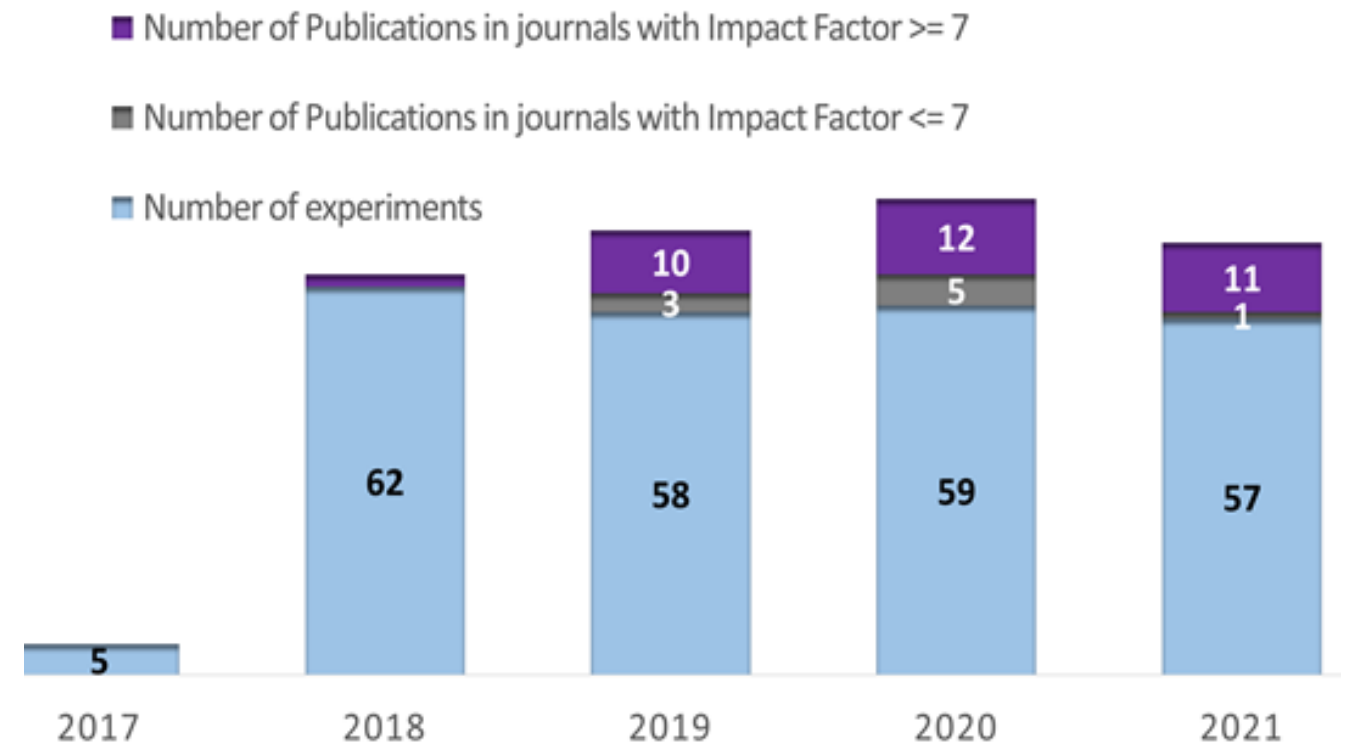
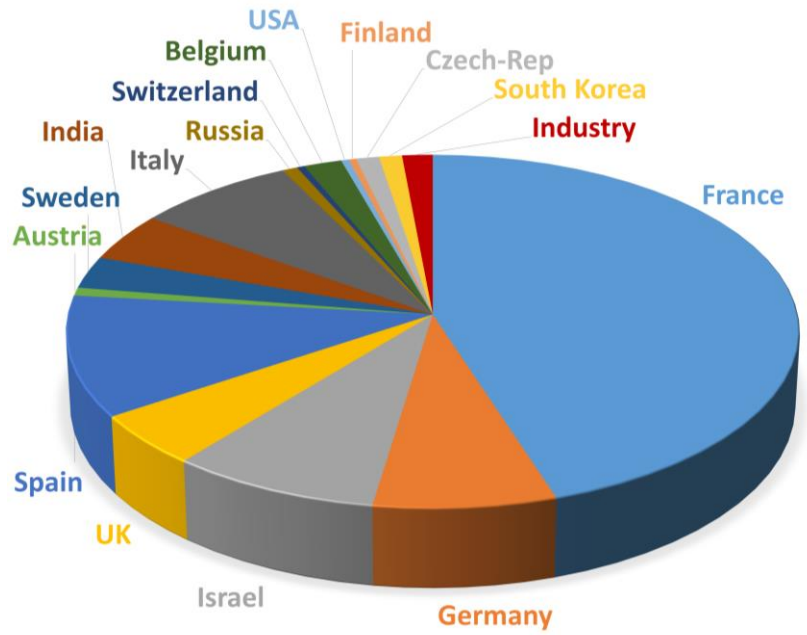
- Titan Krios G3
- Quantum LS energy filter
- K3 direct electron detector
- Volta phase plate



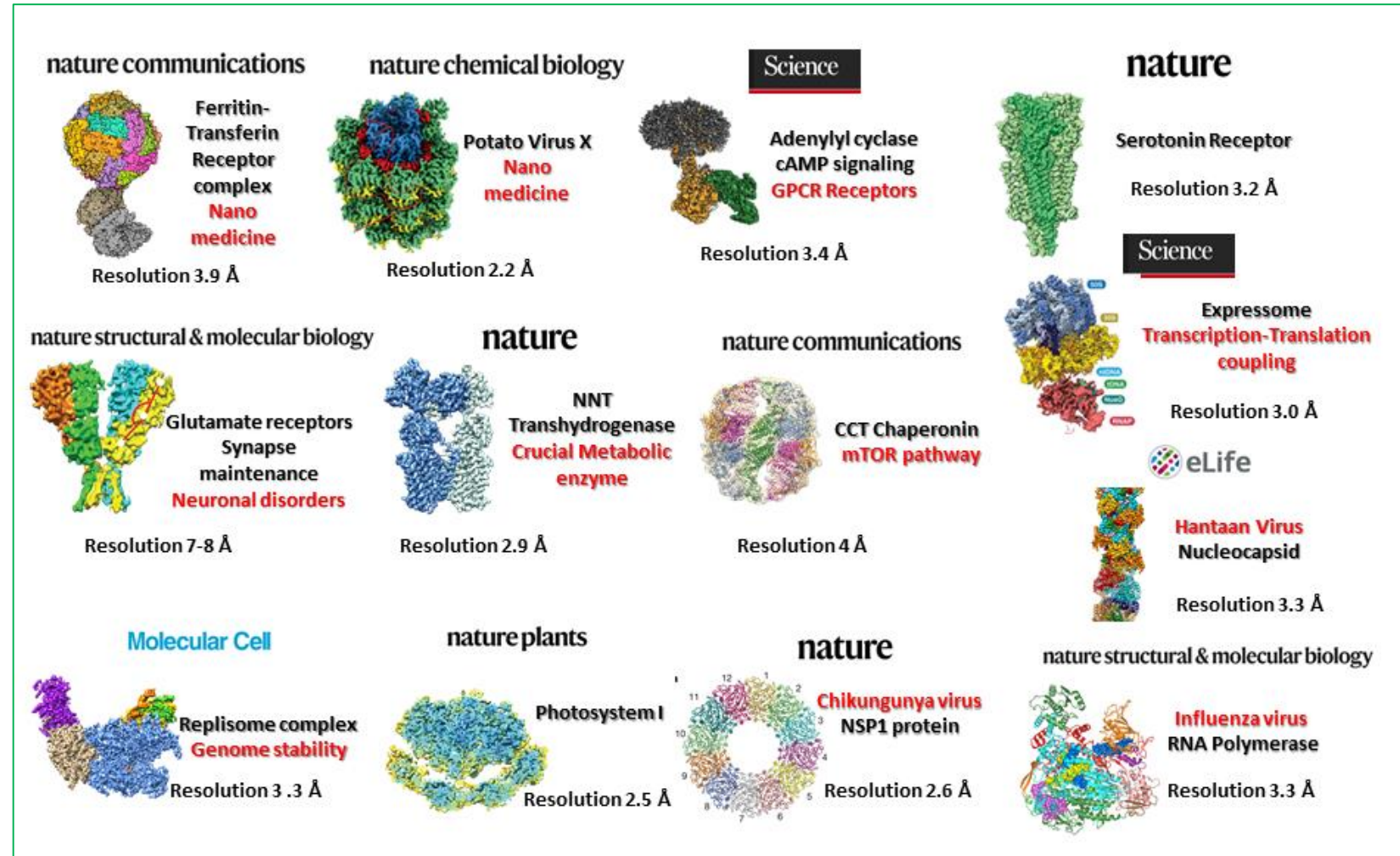
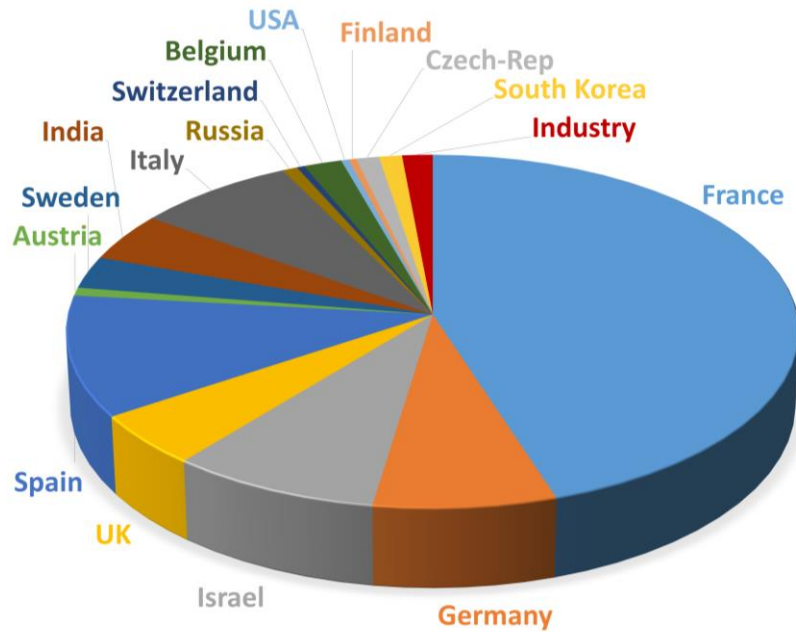
Photo by Cande

- Single particle experiments only
- BAG or Rolling access proposals at any time (direct ESRF submission)
- Rapid access for COVID proposals
- 2 days experiment
- Beam time granted by BTAP (except COVID proposals)
- Pre-characterised samples only (except COVID proposals)

Period: Nov 2017 to Feb 2022



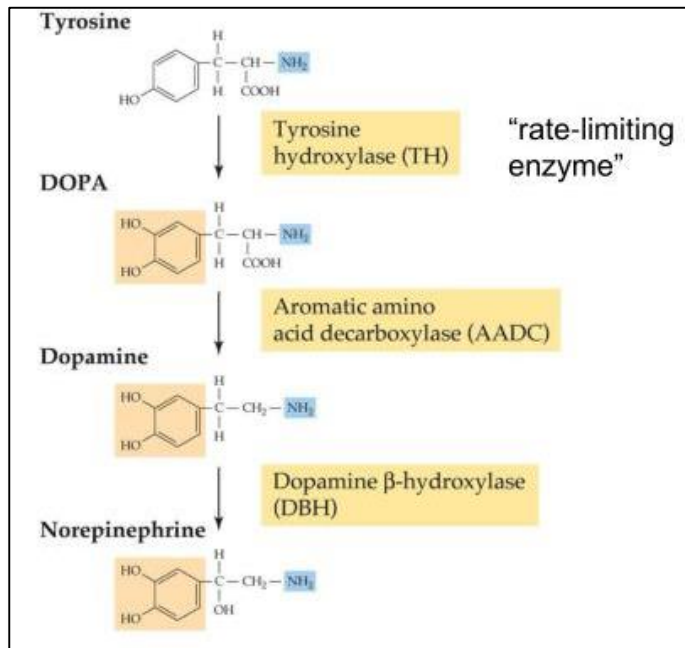
Period: Nov 2017 to Feb 2022



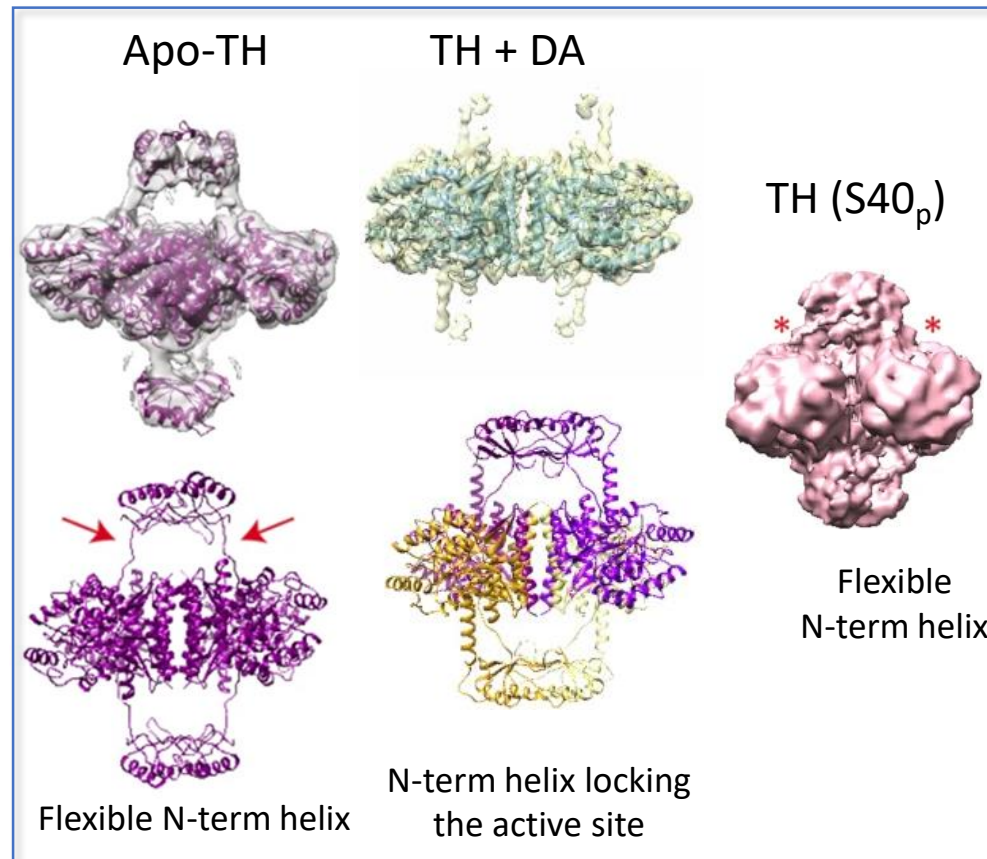
Structural mechanism for tyrosine hydroxylase inhibition by dopamine and reactivation by Ser40 phosphorylation

María Teresa Bueno-Carrasco, ..., José M. Valpuesta , *Nature Communications*, 10th January 2022

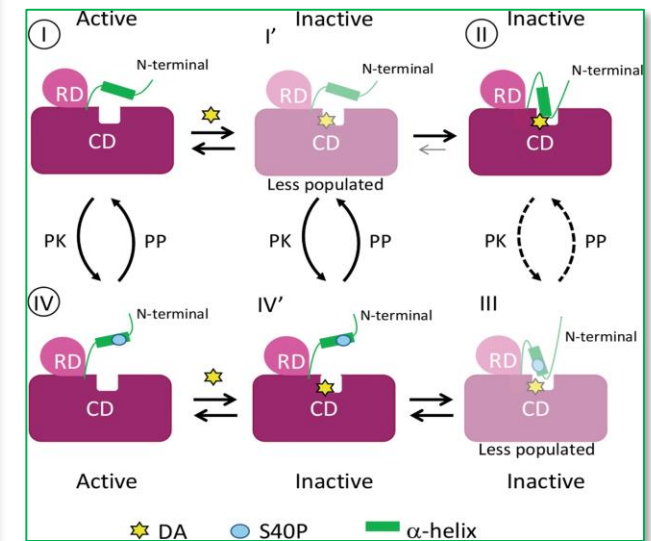
Catecholamines synthesis



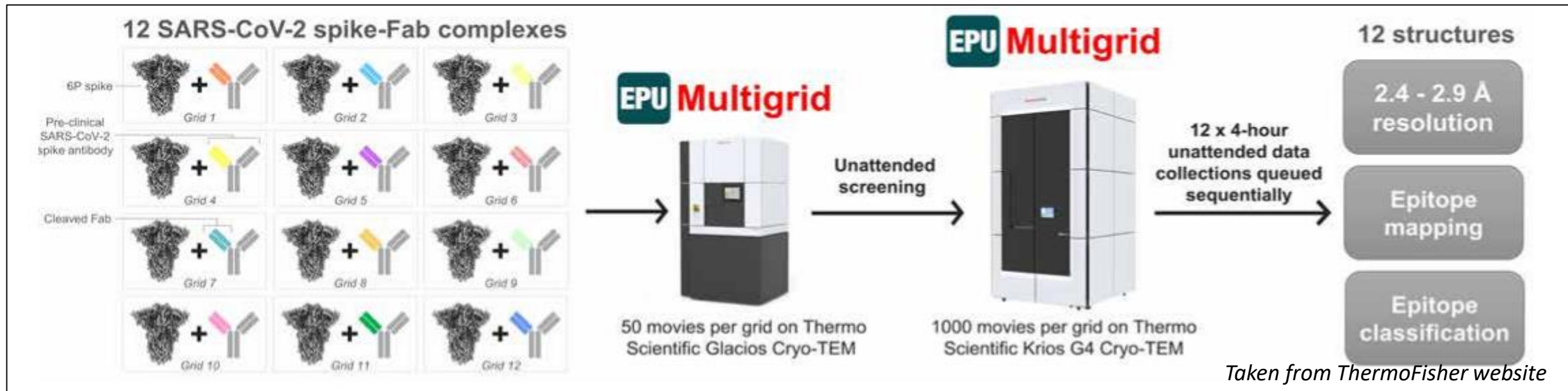
CA deficiency → neurodegenerative disorders
TH deficiency → **hallmark of Parkinson's**



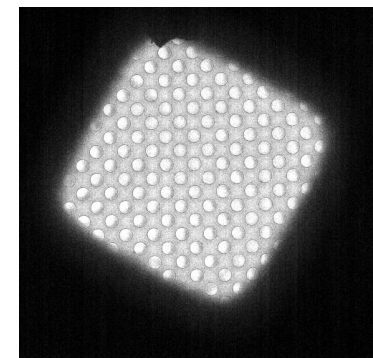
- **Apo state:** TH active → N-terminal helix free to move
- **DA bound state** → TH inhibited due to N-terminal helix locking on the active site → Structural stability
- **S40 phosphorylated state:** N-term helix flexible again → TH active.



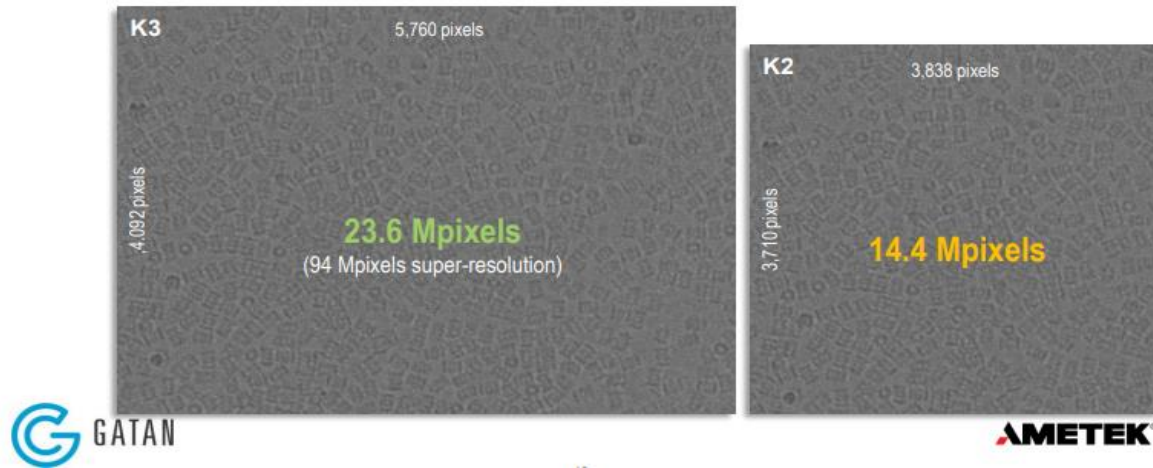
TEM/EPU UPGRADE – MULTIGRID – MULTIPLE SAMPLES



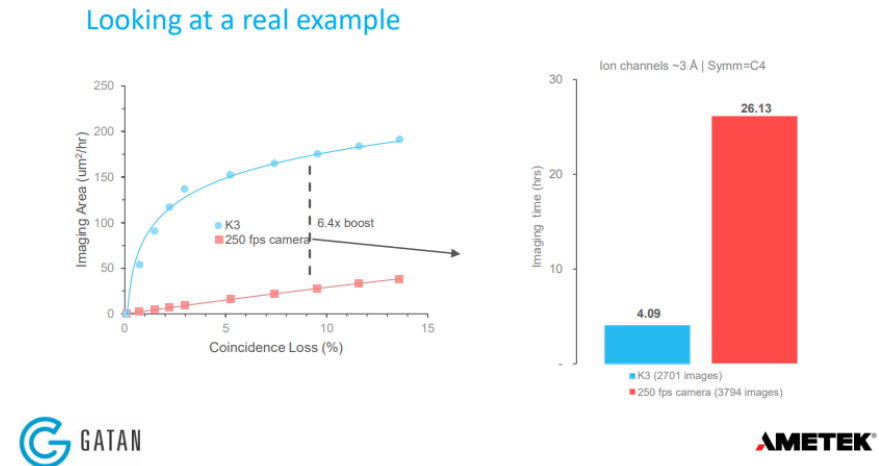
- Multigrid option (**fully automated queue** system)
 - Ideal for **drug screening/epitope mapping**, etc
 - Requires well established sample preparation and data processing methods.
 - Also suitable for **grids with less acquisition area**.
 - Data needs to be combined from several grids. So data processing must be established.
 - This is automated data collection. So, **grid squares should be similar and clean**



1.6X bigger area of acquisition

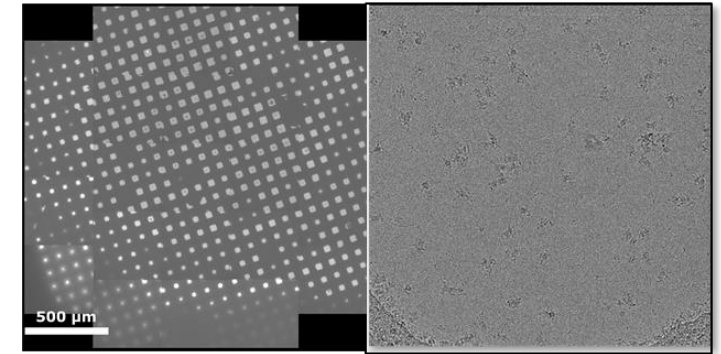


Faster frame rate : higher throughput



- **Speed increase up to 900 images/hour in counting mode** (ideal situation: apoferritin; no contamination, 1 sec exposure, 40 frames, 2um hole size (4 images/hole))
 - **About 10000 images from overnight data collection**
 - **Opens up several possibilities (multiple grids of same sample (ligands/inhibitor/drug, epitope mapping), multiple samples of same user, multiple users (BAG))**
 - **More info soon. Might need friendly BAG to try this first.**

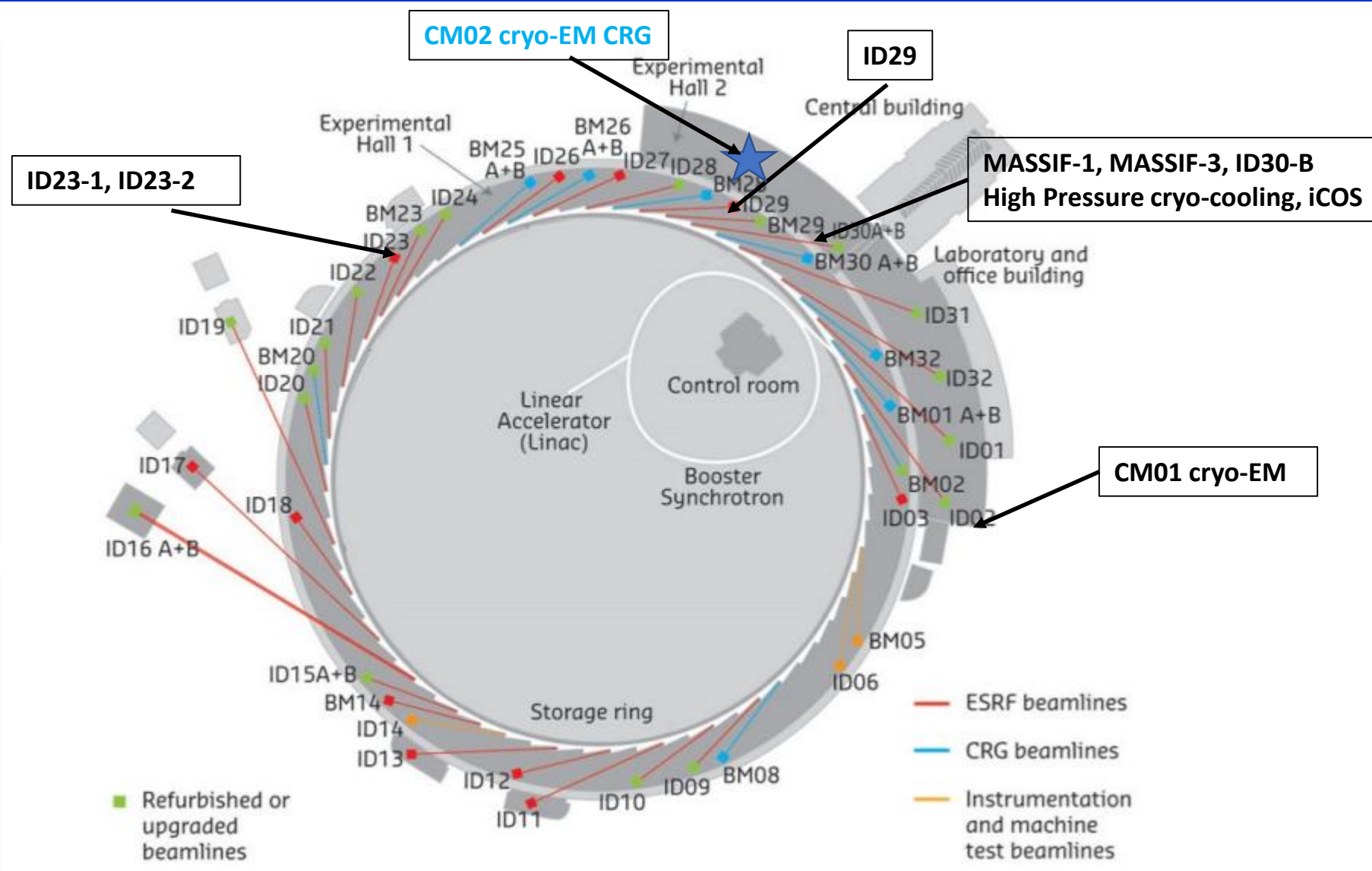
- **PRE-SCREENING of grids → ATLAS is preferable.**
 - For remote users, information on where to collect is useful.
 - help users to gain more beam time.
- **2D classification results from the PRELIMINARY data of the same sample → MANDATORY.**
- **Within 2 weeks from the experiment date, local contacts will contact users for the above details.**
 - Earlier response helps to organize the experiment
- **EARLIER SHIPMENT is MANDATORY.**
 - Avoids loss of Krios beam time.



NEW CRG CRYO-EM BEAMLINE - CM02 – PERSPECTIVES

- Funding from the French national PIA3/Equipex+ initiative.
- State-of-the-art high resolution cryo-EM microscope with energy filter and direct electron detector.
- Will be operated as a CRG beamline in ESRF

- CM02 effect on CM01:**
- **30% extra beamtime**
 - Dissipates users to CM02
 - permits to perform cryo-electron tomography experiments



ESRF

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