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A Research Driven Microscopy Core at New York University Langone Medical Center

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New York University Langone Medical Center (NYULMC) established a new department called the Office of Collaborative Science (OCS) at year of 2010 to oversee and provide support for centralized research cores and shared resource centers. There are a total of 14 cores by now, and all the cores are using the Labvantage LIMS system for instrument sign up, usage record and billing management. With full services provided by professional staff, the core instrument is maintained at the best condition as possible, which will greatly speed up research projects within NYU communities and other institutes. Gained revenue and centralized administration support keeps the core running smoothly. The microscopy core is one of these cores, providing full services for electron microscopy and training, or assist use for light microscopy.

Successful communication with PIs and helping their researches get into a deeper level is the goal of the NYULMC OCS electron microscopy core. By searching in literature, contacting with field experts and cooperating with nearby institutions and the companies, we solved many technical issues and instrumentation problems, and brought in a variety of technologies to the core, including the complicated and newest technologies, such as high-pressure freezing freeze-substitution (HPF-FS) and electron tomography, cryo-electron microscopy, dual beam FIB- scanning electron microscopy and correlative light and electron microscopy. Regular chemical fixation is still a major task for most electron microscopy projects, but special techniques are also involved when the project requested.

One example is our recent work for study the ultra-structure of intercalated disc. To distinguish detailed structure and dynamics of three major components of intercalated disc, including desmosomes, fasciae adherens junctions and gap junctions, is a bit of a challenge for regular chemical fixation method. By using mouse heart prepared by high-pressure freezing and freeze-substitution method as material, we found out that gap junction interacts with components of other complexes, such as mitochondria (Fig. 1) and desmosome (data not shown). In some area, gap junction plaque seems contacting with the outer membrane of mitochondria; inner part of desmosomal plaque is also very closed to the outer membrane of mitochondria (Fig. 1a). The tomography movie indicates that the intercalated disc at mouse heart is very dynamic; there are very strong vesicular activity presented between gap junction and desmosome; those vesicular activities also seem to involve the mitochondria located at both sides of the intercellular space[1] (Fig. 1). Tokuyasu cryo-section immunolocalization confirmed that Cx43, a major component of gap junction could be in physical contacted with the molecular components of other structure (Fig. 2). Further studies were performed using HPF-FS method prepared mouse heart from both wild type and shRNA-mediated loss of the desmosomal protein plakophilin-2 (*pkp2*). Tomographic images of wild type (Fig. 3a) and PKP2-Heterozygous-null (Fig. 3b) mice, revealed the sporadic or loss of desmosome, non-uniform and enlarged intracellular membrane space of the PKP2-Hz mouse[2] (Fig. 3a and 3b), which may be the reason for Arrhythmogenic Cadiomyopathy[3].

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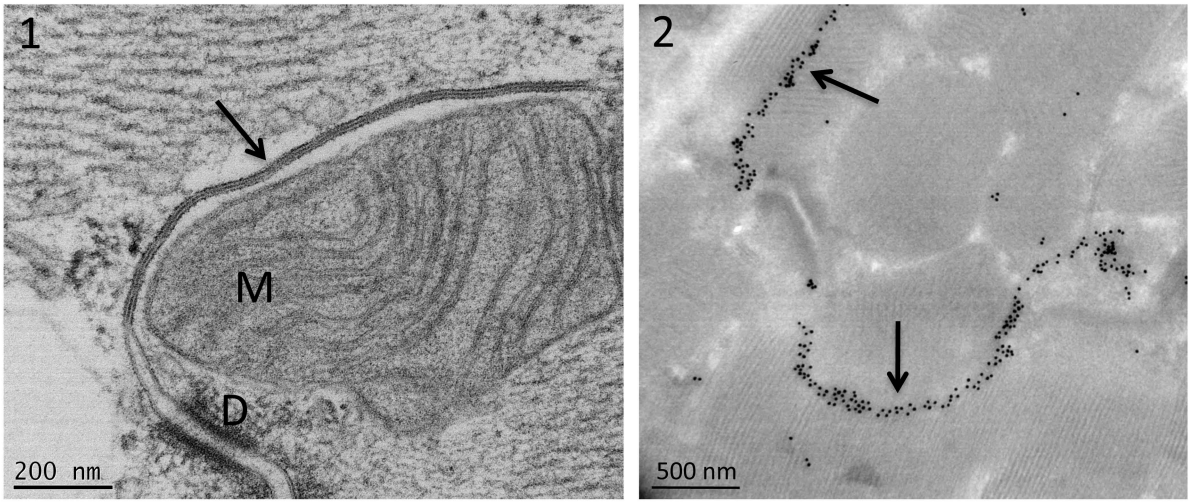

Figure 1. Murine heart prepared by high-pressure freezing and freeze-substitution method. Note mitochondria (M) is very closed to gap junction (arrow). D represents desmosome.

Figure 2. Cryo-immunoelectron microscopy shows Cx43 localization at gap junction (arrow) of murine heart.

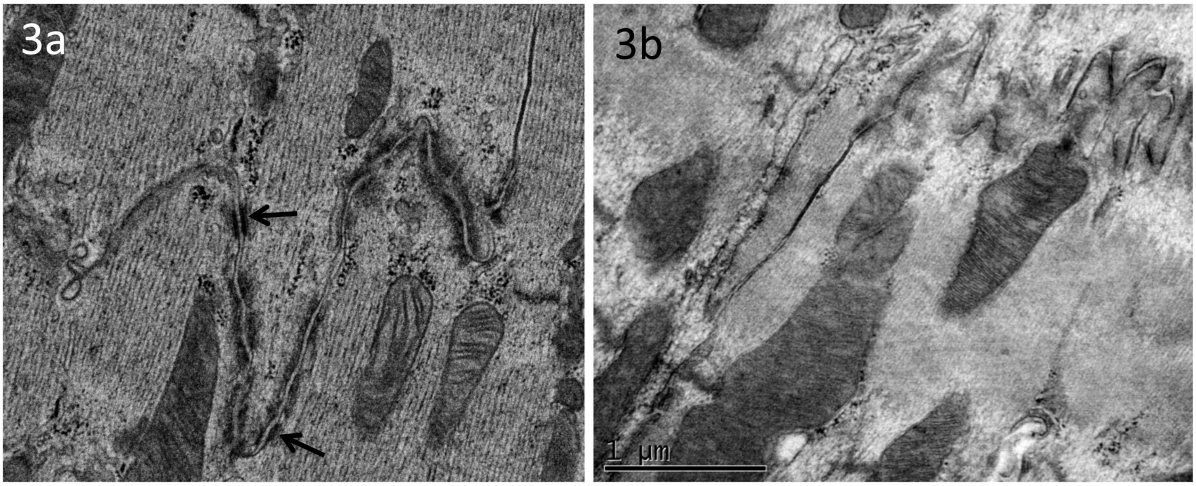

Figure 3. Intercalated disc of wild type (Fig. 3a) and PKP2-Hz mouse (Fig. 3b). Note the lack of desmosome (D) and irregular intracellular space at PKP2-Hz murine heart (Fig. 3b).

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