



POSTER PRESENTATION

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# Molecular and morphological characterization of piecemeal degranulation in human neutrophil azurophilic granules

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Mediators pre-stored in neutrophil azurophilic granules are central to the acute inflammatory response and tissue degradation and damage through their proteolytic activity. Different granule populations mobilize and release their content via distinct and hierarchical molecular mechanisms. The molecular mechanisms by which mediators pre-stored in azurophilic granules are mobilized and released to the extracellular space remain largely unknown. We used a number of complementary techniques including; confocal laser scanning microscopy, subcellular fractionation, flow cytometric analyses, Western blot analyses and electron microscopy to examine the ultrastructural and molecular nature of mediator release in neutrophil azurophilic granules. We found that following IL-8 activation, neutrophil azurophilic granules undergo piecemeal degranulation (selective mediator release) leading to altered granule content. Piecemeal degranulation of azurophilic granules is characterized by budding of small secretory vesicles and consequent reduction in granule density. Furthermore, budding of small secretory vesicles and selective mediator mobilization and release from azurophilic granules is associated with reduced localization of CD63, Hck and  $\beta$ -arrestin-1 to granule membranes and also cell surface upregulation of these molecules. Our study is first to identify piecemeal degranulation as a potential underlying mechanism of mediator release from neutrophil azurophilic granules and supports the involvement of CD63, Hck, and  $\beta$ -arrestin-1 in this process.

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