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Novel fluorescent molecular sensors as multitasking molecules for cell imaging and metal ion detection

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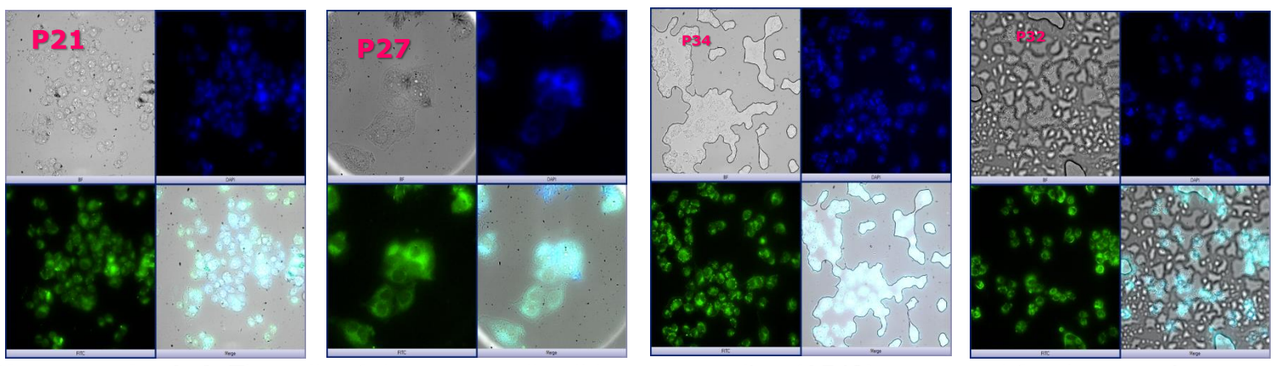
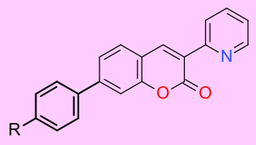
The invention relates to the development of new fluorescent dyes derived from 3- (2-pyridyl) chromen-2-one which are suitable for **biological studies using fluorescence microscopy or confocal microscopy.** The developed fluorescent markers penetrate inside the cells through the cell membrane and, which is extremely important from the application point of view, selectively connect with specific cell structures and at the same time emit fluorescence light of a specific color (i.e. a specific wavelength). The use of coumarin derivatives as fluorescent dyes allows for the labeling of individual cell organelles and the monitoring of chemical processes inside the cell in-situ and on-line. Thus, the use of these sensors to image cell organelles could be a breakthrough in medicine. **It may contribute to the early diagnosis of neoplastic changes and the reduction of resection of healthy tissues during surgical procedures**. In addition, coumarin derivatives are suitable for the selective and sensitive determination of albumin protein concentration, which is extremely important for the proper functioning of the body. Too high or low levels of albumin can indicate kidney or liver damage.

Fluorescent Sensors for Biomedical Diagnostics – Bio-Imaging Sensor

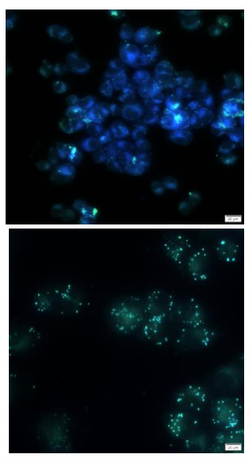


Photographs 1-4. The cells of the non-small cell lung cancer line (A549) were used for the experiments. Cells were grown under standard conditions (5% CO_2 atmosphere, 37 ° C) in DMEM F12 medium supplemented with 10% bovine serum and antibiotics in culture vessels of the area 25 cm^2. The cells were then seeded for multi-well plates (12-well plates) at a density of 10,000 cells / well for the purposes of the experiment. The analysis was carried out using a an inverted fluorescence microscope Olympus IX83 equipped with X-line lenses and a monochrome camera Photometrics Prime BSI.

3-(2-pyridyl) chromen-2-one derivatives



P21 H
P26 F
P25 CH_3
P28 CF_3
P29 OCH_3
P31 OH
P32 NO_2
P27 CN
P34 SO_2CH_3



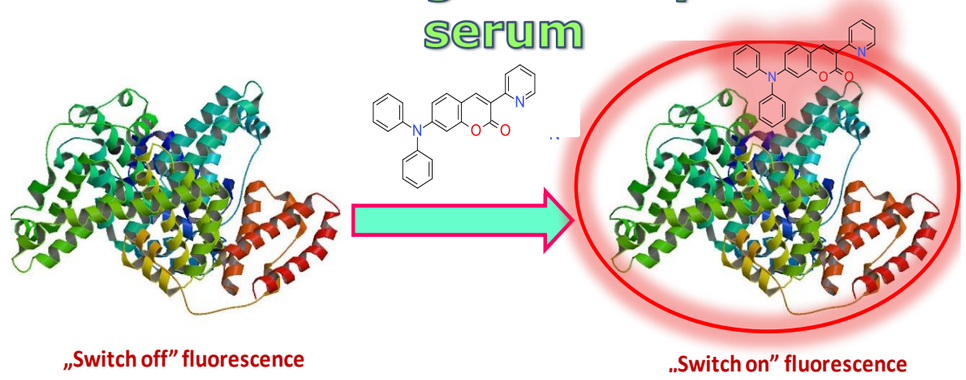
The study used a non-small cell lung cancer line

3-(2-pyridyl) chromen-2-one derivatives

Pat.239829
Pat.239830

(2021-10-20)

Optical Sensors for Biomedical Diagnostics - hydrophobic fluorescent probe for albumin binding sites in plasma and serum



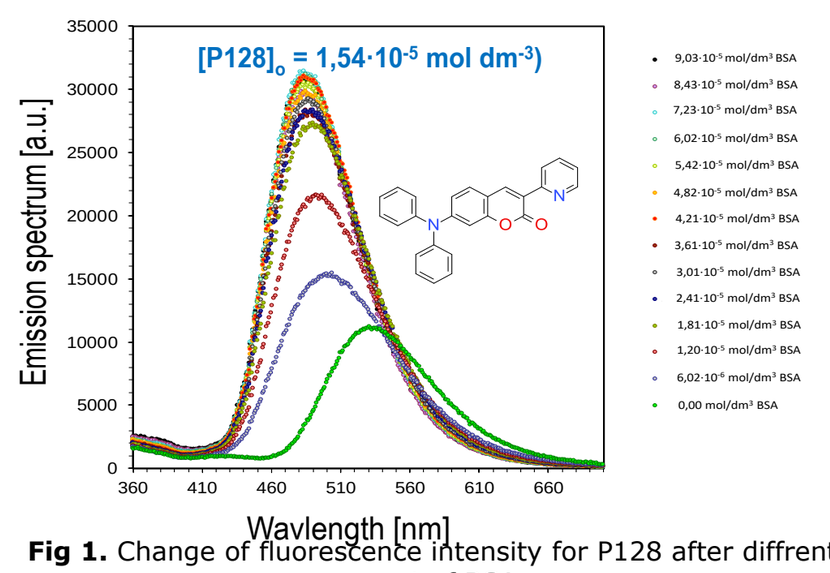
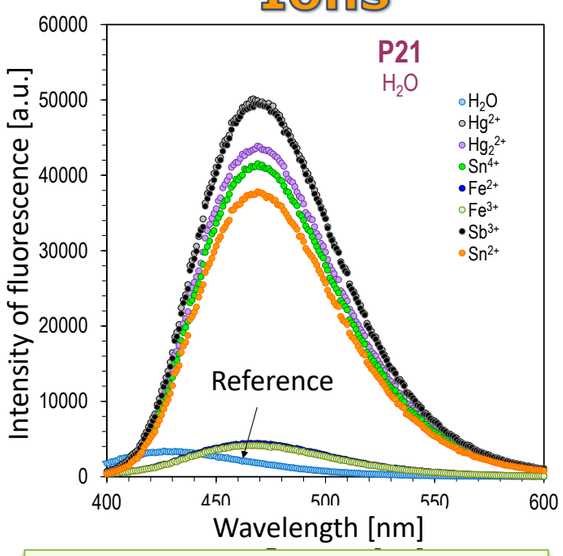


Fig 1. Change of fluorescence intensity for P128 after diffrent amout of BSA.

Fluorescent Sensors for Measuring Metal Ions



Hg^{2+} Hg$_2^{2+}$, Fe^{2+}, Fe^{3+}, Sb^{3+}, Sn^{4+}, Sn^{2+}

Fig 2. Change of fluorescence intensity for P21 after ion addition.

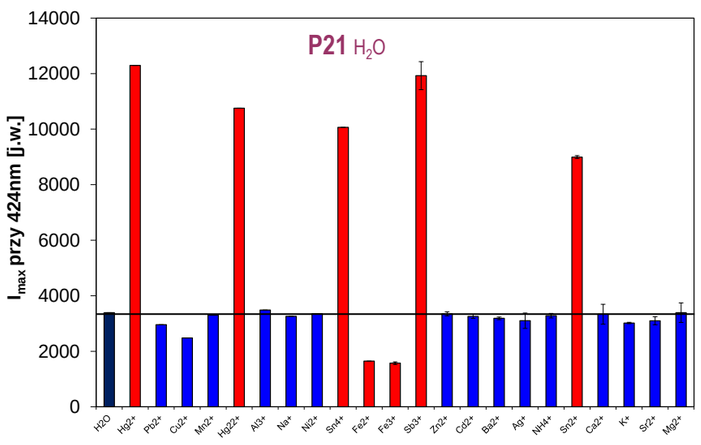


Fig.3. Comparison of changes in the fluorescence intensity of the emission spectrum maximum for compound P21 in water after the addition of various ions in relation to the reference - 21 compound in water (black bar).

Safe and Non-Toxic Optical Sensors for Biomedical Diagnostics

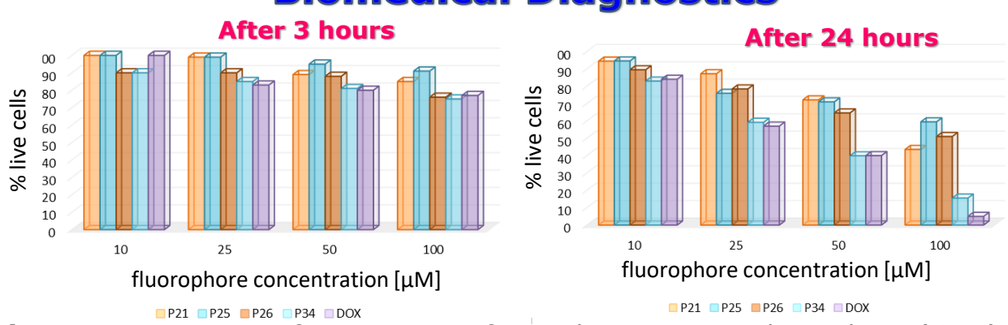
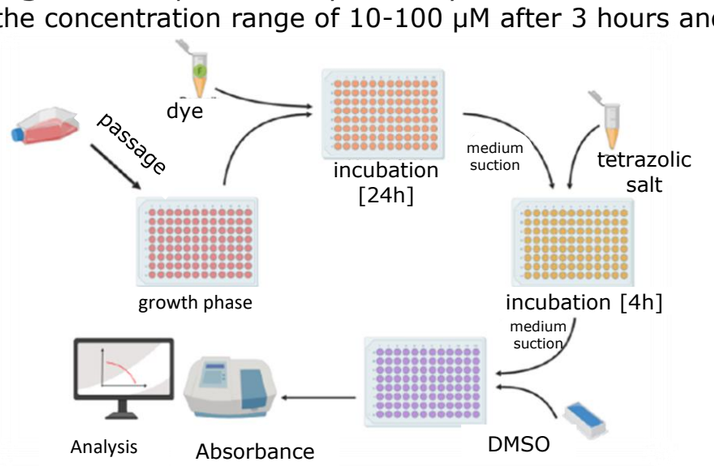


Fig 4-5. Comparison of cytotoxicity of tested coumarin to doxorubicin (DOX) in the concentration range of 10-100 μM after 3 hours and 24 hours of incubation.



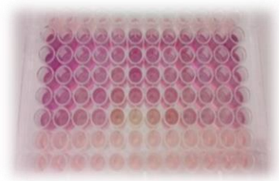


Fig.6. Principle of testing cytotoxicity.

As part of the invention, new, safe fluorescent dyes have been developed that selectively associate with specific cell structures, which allows the monitoring of chemical processes inside the cell in-situ and on-line, and thus also allows monitoring any changes occurring in the body. These compounds can be used as a medical device in the diagnosis of diseases, and for molecular bioimaging using fluorescence and confocal microscopy. Potential recipients can be companies such as: Genomed S.A, Evitum - Professional Diagnostic Center, ZEISS, ThermoFisher, OLYMPUS, nikon, ILIXA image biopsy lab and many others.

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BENEFITS

These compounds have important advantages as molecular luminescent sensors:
✓ Non-toxic;
✓ Excellent chemical stability;
✓ Excellent luminescence properties;
✓ Very long lifetimes;

INDUSTRIAL APPLICATIONS

This innovation could be used for:
✓ Fluorescence imaging – cell visualization, fluorescence probe technology,time-resolved chemical and biological analysis
✓ Detection biologically and/or environmentally important cations, anions, small neutral molecules as well as biomacromolecules (such as proteins and DNA).